

Reactive arthritis is associated with which one of the following HLA antigens?

☒	HLA-B27
☐	HLA-A3
☐	HLA-DR4
☐	HLA-B5
☐	HLA-DR3

Submit answer

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Reactive arthritis

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

Epidemiology

- post-STI form much more common in men (e.g. 10:1)
- post-dysenteric form equal sex incidence

<i>Shigella flexneri</i> <i>Salmonella typhimurium</i> <i>Salmonella enteritidis</i> <i>Yersinia enterocolitica</i> <i>Campylobacter</i>	<i>Chlamydia trachomatis</i>
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Management

- symptomatic: analgesia, NSAIDS, intra-articular steroids
- sulfasalazine and methotrexate are sometimes used for persistent disease
- symptoms rarely last more than 12 months

A 47-year-old man with a history of chronic sinusitis presents with shortness of breath to the Emergency Department. Initial investigations reveal:

Hb	10.4g/dl
Platelets	$477 \times 10^9/l$
WCC	$14.3 \times 10^9/l$
ESR	92 mm/h
Urea	20 mmol/l
Creatinine	198 $\mu\text{mol/l}$
Urine dipstick	blood +++

What is the most likely diagnosis?

☐	Mixed cryoglobulinaemia
☐	Churg-Strauss syndrome
☐	Wegener's granulomatosis Granulomatosis with polyangiitis
☐	Haemolytic uraemic syndrome
☐	Henoch-Schonlein purpura

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The combination of pulmonary and renal involvement combined with a history of chronic sinusitis points towards a diagnosis of Wegener's granulomatosis.

Wegener's granulomatosis

Wegener's granulomatosis is an autoimmune condition associated with a necrotizing granulomatous vasculitis, affecting both the upper and lower respiratory tract as well as the kidneys.

Features

- upper respiratory tract: epistaxis, sinusitis, nasal crusting
- lower respiratory tract: dyspnoea, haemoptysis
- rapidly progressive glomerulonephritis ('pauci-immune', 80% of patients)
- saddle-shape nose deformity
- also: vasculitic rash, eye involvement (e.g. proptosis), cranial nerve lesions

Investigations

- cANCA positive in > 90%, pANCA positive in 25%
- chest x-ray: wide variety of presentations, including cavitating lesions
- renal biopsy: epithelial crescents in Bowman's capsule

Management

- steroids
- cyclophosphamide (90% response)
- plasma exchange
- median survival = 8-9 years

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**Granulomatosis with
polyangiitis (Wegener's
granulomatosis)**

Renal failure

Epistaxis /
haemoptysis

cANCA

Vasculitis

Sinusitis

Dyspnoea

**Churg-Strauss
syndrome**

Asthma

pANCA

Eosinophilia

A 50-year-old female with a history of rheumatoid presents with a suspected septic knee joint. A diagnostic aspiration is performed and sent to microbiology. Which of the following organisms is most likely to be responsible?

☐	<i>Staphylococcus aureus</i>
☐	<i>Staphylococcus epidermidis</i>
☐	<i>Escherichia coli</i>
☐	<i>Neisseria gonorrhoeae</i>
☐	<i>Streptococcus pneumoniae</i>

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Staphylococcus aureus



Staphylococcus epidermidis



Escherichia coli



Neisseria gonorrhoeae



Streptococcus pneumoniae

Septic arthritis

Overview

- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

Management

- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

Low levels of which one of the following types of complement are associated with the development of systemic lupus erythematosus?

☐	C4
☐	C5
☐	C6
☐	C7
☐	C8

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☐	C7
☐	C8

Submit answer

Low levels of C4a and C4b have been shown to be associated with an increased risk of developing systemic lupus erythematosus

SLE: investigations

Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)
- also: anti-U1 RNP, SS-A (anti-Ro) and SS-B (anti-La)

Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

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Which one of the following is not a risk factor for developing osteoporosis?

☐	Smoking
☐	Obesity
☐	Sedentary lifestyle
☐	Premature menopause
☐	Female sex

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Low body mass, rather than obesity is associated with an increased risk of developing osteoporosis

Osteoporosis: causes

Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

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There are many other risk factors and secondary causes of osteoporosis. We'll start by looking at the most 'important' ones - these are risk factors that are used by major risk assessment tools such as FRAX:

- history of glucocorticoid use
- rheumatoid arthritis
- alcohol excess
- history of parental hip fracture
- low body mass index
- current smoking

Other risk factors

- sedentary lifestyle

- premature menopause

Caucasians and Asians

- endocrine disorders: hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus

- multiple myeloma, lymphoma

- gastrointestinal disorders: inflammatory bowel disease, malabsorption (e.g. Coeliac's), gastrectomy, liver disease

- chronic kidney disease

- osteogenesis imperfecta, homocystinuria

Medications that may worsen osteoporosis (other than glucocorticoids):

- SSRIs

- antiepileptics

- proton pump inhibitors

- glitazones

- long term heparin therapy

- aromatase inhibitors e.g. anastrozole

A health trust in the United Kingdom which serves a population of 100,000 is planning services for patients with rheumatoid arthritis. How many of the population would be expected to have the disease?

☐	100
☐	300
☐	1,000
☐	2,000
☐	10,000

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The prevalence of rheumatoid arthritis in the UK population is approximately 1%

Rheumatoid arthritis: epidemiology

Epidemiology

- peak onset = 30-50 years, although occurs in all age groups
- F:M ratio = 3:1
- prevalence = 1%
- some ethnic differences e.g. high in Native Americans
- associated with HLA-DR4 (especially Felty's syndrome)

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A 31-year-old female intolerant of methotrexate is started on azathioprine for rheumatoid arthritis. Routine blood monitoring shows:

Hb	7.9 g/dl
Plt	$97 \times 10^9/l$
WBC	$2.7 \times 10^9/l$

Which of the following factors will predispose her to azathioprine toxicity?

☐	Cimetidine
☐	Rifampicin
☐	Fast acetylator status
☐	Thiopurine methyltransferase deficiency
☐	Alcohol excess

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د. محمد وراز ©

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Azathioprine - check thiopurine methyltransferase deficiency (TPMT) before treatment

Thiopurine methyltransferase (TPMT) deficiency is present in about 1 in 200 people and predisposes to azathioprine related pancytopenia

Azathioprine

Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits purine synthesis. A thiopurine methyltransferase (TPMT) test may be needed to look for individuals prone to azathioprine toxicity.

Adverse effects include

- bone marrow depression
- nausea/vomiting
- pancreatitis

A significant interaction may occur with allopurinol and hence lower doses of azathioprine should be used.

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Which of the following features are not typically seen in a patient with adult onset Still's disease?

☐	Maculopapular rash
☐	Rheumatoid factor
☐	Pyrexia
☐	High ferritin level
☐	Lymphadenopathy

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د. عاصم وراز ©

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Adult onset Still's disease is typically rheumatoid factor negative

Still's disease in adults

Adult Still's disease

- typically affects 16-35 year olds

Features

- arthralgia
- elevated serum ferritin
- rash: salmon-pink, maculopapular
- pyrexia
- lymphadenopathy
- rheumatoid factor (RF) and anti-nuclear antibody (ANA) negative

A 34-year-old woman with a history of antiphospholipid syndrome presents with a swollen and painful leg. Doppler ultrasound confirms a deep vein thrombosis (DVT). She had a previous DVT 4 months ago and was taking warfarin (with a target INR of 2-3) when the DVT occurred. How should her anticoagulation be managed?

- | | |
|-----------------------|--|
| ☐ | Life-long warfarin, increase target INR to 3 - 4 |
| ☐ | Add in life-long low-dose aspirin |
| ☐ | A further 6 months warfarin, target INR 2 - 3 |
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Submit answer

The evidence base is scanty here but most clinicians would increase the target INR to 3-4 if a patient has had a further thrombosis with an INR of 2-3. Please see the BCSH guidelines

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

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A 41-year-old man with a past history of asthma presents with pain and weakness in his left hand. Examination findings are consistent with a left ulnar nerve palsy. Blood tests reveal an eosinophilia. Which one of the following antibodies is most likely to be present?

☐	ANA
☐	Anti-Scl70
☐	pANCA
☐	Antiphospholipid antibodies
☐	cANCA

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Submit answer

This patient has Churg-Strauss syndrome as evidenced by the asthma, mononeuritis and eosinophilia

Churg-Strauss syndrome

Churg-Strauss syndrome is an ANCA associated small-medium vessel vasculitis.

Features

- asthma
- blood eosinophilia (e.g. > 10%)
- paranasal sinusitis
- mononeuritis multiplex
- pANCA positive in 60%

Leukotriene receptor antagonists may precipitate the disease

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A 34-year-old intravenous drug user is admitted with a purpuric rash affecting her legs. Blood tests reveal the following:

Hb	11.4g/dl
Platelets	$489 \times 10^9/l$
WCC	$12.3 \times 10^9/l$
HCV PCR	positive
HBsAg	negative
Rheumatoid factor	positive
C3/C4	reduced

What is the most likely diagnosis?

☐	Polyarteritis nodosa
☐	Henoch-Schonlein purpura
☐	Wegener's granulomatosis
☐	Cryoglobulinaemia
☐	Systemic lupus erythematosus

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Hepatitis C infection is associated with type II (mixed) cryoglobulinaemia, suggested by the purpuric rash, positive rheumatoid factor and reduced complement levels

Cryoglobulinaemia

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C.
One third of cases are idiopathic

Three types

- type I (25%): monoclonal
- type II (25%): mixed monoclonal and polyclonal: usually with RF
- type III (50%): polyclonal: usually with RF

Type I

- monoclonal - IgG or IgM
- associations: multiple myeloma, Waldenström macroglobulinaemia

Type II

- mixed monoclonal and polyclonal: usually with RF
- associations: hepatitis C, RA, Sjogren's, lymphoma

Type III

- polyclonal: usually with RF
- associations: RA, Sjogren's

Symptoms (if present in high concentrations)

- Raynaud's only seen in type I
- cutaneous: vascular purpura, distal ulceration, ulceration
- arthralgia
- renal involvement (diffuse glomerulonephritis)

Tests

- low complement (esp. C4)
- high ESR

Treatment

- immunosuppression
- plasmapheresis

A 59-year-old man with a history of gout presents with a swollen and painful first metatarsophalangeal joint. He currently takes allopurinol 400mg od as gout prophylaxis. What should happen to his allopurinol therapy?

☐	Stop and recommence 4 weeks after acute inflammation has settled
☐	Reduce allopurinol to 100mg od until acute attack has settled
☐	Stop and switch to colchicine prophylaxis
☐	Stop and recommence 2 weeks after acute inflammation has settled
☐	Continue allopurinol in current dose

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Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 $\mu\text{mol/l}$)

Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine* has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol**

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

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A 34-year-old is diagnosed with chronic fatigue syndrome. Which one of the following interventions is most useful?

☐	Graded exercise therapy
☐	Psychodynamic psychotherapy
☐	Graded physiotherapy
☐	Advice to avoid alcohol and caffeine
☐	Low-dose fluoxetine

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Chronic fatigue syndrome

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

Epidemiology

- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include

- sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep-wake cycle
- muscle and/or joint pains
- headaches
- painful lymph nodes without enlargement
- sore throat
- cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
- physical or mental exertion makes symptoms worse
- general malaise or 'flu-like' symptoms
- dizziness
- nausea
- palpitations

Investigation

- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin*, coeliac screening and also urinalysis

Management

- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

*children and young people only

A 68-year-old female presents with a two week history of intermittent headaches and lethargy. Blood tests reveal the following:

ESR	67 mm/hr
-----	----------

What is the most likely diagnosis?

☐	Polymyalgia rheumatica
☐	Cluster headaches
☐	Polyarteritis nodosa
☐	Migraine
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This is a classic history of temporal arteritis. Treatment should be started immediately with high dose steroids (e.g. prednisolone 1mg/kg/day) to reduce the chance of visual loss

Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

Treatment

- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible

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Which one of the following cytokines is the most important in the pathophysiology of rheumatoid arthritis?

☐	IFN-beta
☐	IFN-alpha
☐	IL-4
☐	Tumour necrosis factor
☐	IL-2

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Tumour necrosis factor

Tumour necrosis factor (TNF) is a pro-inflammatory cytokine with multiple roles in the immune system

TNF is secreted mainly by macrophages and has a number of effects on the immune system, acting mainly in a paracrine fashion:

- activates macrophages and neutrophils
- acts as costimulator for T cell activation
- key mediator of bodies response to Gram negative septicaemia
- similar properties to IL-1
- anti-tumour effect (e.g. phospholipase activation)

TNF-alpha binds to both the p55 and p75 receptor. These receptors can induce apoptosis. It also cause activation of NFkB

Endothelial effects include increase expression of selectins and increased production of platelet activating factor, IL-1 and prostaglandins

TNF promotes the proliferation of fibroblasts and their production of protease and collagenase. It is thought fragments of receptors act as binding points in serum

Systemic effects include pyrexia, increased acute phase proteins and disordered metabolism leading to cachexia

TNF is important in the pathogenesis of rheumatoid arthritis - TNF blockers (e.g. infliximab, etanercept) are now licensed for treatment of severe rheumatoid

TNF blockers

- infliximab: monoclonal antibody, IV administration
- etanercept: fusion protein that mimics the inhibitory effects of naturally occurring soluble TNF receptors, subcutaneous administration
- adalimumab: monoclonal antibody, subcutaneous administration
- adverse effects of TNF blockers include reactivation of latent tuberculosis and demyelination

Infliximab is also used in active Crohn's disease unresponsive to steroids

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A 54-year-old female is reviewed in the rheumatology clinic due to dry eyes and arthralgia. A diagnosis of primary Sjogren's syndrome is suspected. Which one of the following features is least associated with this condition?

☐	Renal tubular acidosis
☐	Xerostomia
☐	Sensory polyneuropathy
☐	Dilated cardiomyopathy
☐	Raynaud's phenomenon

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Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management

- artificial saliva and tears
- pilocarpine may stimulate saliva production

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Which one of the following statements regarding systemic lupus erythematosus is true?

☐	It is linked with HLA A5
☐	Onset is typically between 20-40 years old
☐	It is more common in Caucasians
☐	The female:male ratio is 3:1
☐	The incidence has decreased in the past 30 years

Submit answer

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Submit answer

د. جاسع وراز ©

Systemic lupus erythematosus

Epidemiology

- much more common in females (F:M = 9:1)
- more common in Afro-Caribbeans* and Asian communities
- onset is usually 20-40 years
- incidence has risen substantially during the past 50 years (3 fold using American College of Rheumatology criteria)

Pathophysiology

- autoimmune disease
- associated with HLA B8, DR2, DR3
- thought to be caused by immune system dysregulation leading to immune complex formation
- immune complex deposition can affect any organ including the skin, joints, kidneys and brain

*It is said the incidence in black Africans is much lower than in black Americans - the reasons for this are unclear

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A 45-year-old female with a history of rheumatoid arthritis presents to the Emergency Department with a two day history of a hot, painful, swollen right elbow joint. What is the most appropriate management?

☐	Joint aspiration
☐	Start infliximab
☐	Oral high-dose prednisolone
☐	Short course of methotrexate
☐	Depomedrone injection

Submit answer

د. حاصی وراز ©

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Joint aspiration is mandatory in all patients with a hot, swollen joint to rule out septic arthritis. If this was excluded in the above patient then intra-articular or system steroid therapy may be considered.

Septic arthritis

Overview

- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

Management

- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

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A 45-year-old man presents with a painful swelling on the posterior aspect of his elbow. There is no history of trauma. On examination an erythematous tender swelling is noted. What is the most likely diagnosis?

☐	Synovial cyst
☐	Haemarthrosis
☐	Septic arthritis
☐	Gout
☐	Olecranon bursitis

Submit answer

د. عاصم وراز ©

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Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

Lateral epicondylitis (tennis elbow)	Features • pain and tenderness localised to the lateral epicondyle • pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended • episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks
Medial epicondylitis (golfer's elbow)	Features • pain and tenderness localised to the medial epicondyle • pain is aggravated by wrist flexion and pronation • symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement
Radial tunnel syndrome	Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse. Features • symptoms are similar to lateral epicondylitis making it difficult to diagnose • however, the pain tends to be around 4-5 cm distal to the lateral epicondyle • symptoms may be worsened by extending the elbow and pronating the forearm
Cubital tunnel syndrome	Due to the compression of the ulnar nerve. Features • initially intermittent tingling in the 4th and 5th finger • may be worse when the elbow is resting on a firm surface or flexed for extended periods • later numbness in the 4th and 5th finger with associated weakness
Olecranon bursitis	Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.

Which one of the following features is least commonly seen in drug-induced lupus?

☐	Glomerulonephritis
☐	Arthralgia
☐	Myalgia
☐	Malar rash
☐	Pleurisy

Submit answer

د. حاصیہ وراز ©

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Submit answer

د. جاسم وراز ©

Glomerulonephritis is unusual in drug-induced lupus

Drug-induced lupus

In drug-induced lupus not all the typical features of systemic lupus erythematosus are seen, with renal and nervous system involvement being unusual. It usually resolves on stopping the drug.

Features

- arthralgia
- myalgia
- skin (e.g. malar rash) and pulmonary involvement (e.g. pleurisy) are common
- ANA positive in 100%, dsDNA negative
- anti-histone antibodies are found in 80-90%
- anti-Ro, anti-Smith positive in around 5%



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A woman with drug-induced lupus

Most common causes

- procainamide
- hydralazine

Less common causes

- isoniazid
- minocycline
- phenytoin

Which of the following is associated with a good prognosis in rheumatoid arthritis?

☐	Rheumatoid factor negative
☐	HLA DR4
☐	Anti-CCP antibodies
☐	Rheumatoid nodules
☐	Insidious onset

Submit answer

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Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

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A 64-year-old man with chronic kidney disease stage 3 secondary to type 2 diabetes mellitus presents with pain and swelling at the right first metatarsophalangeal joint. On examination the joint is hot, erythematous and tender to touch, although he can still flex the big toe. What is the most appropriate initial management?

☐	Colchicine
☐	Prednisolone
☐	Co-codamol 30/500
☐	Allopurinol
☐	Indomethacin

Submit answer

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Submit answer

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Colchicine is useful in patients with renal impairment who develop gout as NSAIDs are relatively contraindicated. The BNF advises to reduce the dose by up to 50% if creatinine clearance is less than 50 ml/min and to avoid if creatinine clearance is less than 10 ml/min.

Co-codamol 30/500 may be used as an adjunct but would not provide relief as monotherapy.

Prednisolone is an option but would adversely affect his diabetic control.

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 $\mu\text{mol/l}$)

Acute management

- NSAIDs
 - intra-articular steroid injection
 - colchicine* has a slower onset of action. The main side-effect is diarrhoea
 - if the patient is already taking allopurinol it should be continued
- oral steroids may be considered if NSAIDs and colchicine are contraindicated. A dose of prednisolone 15mg/day is usually used

Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol**

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

Other points

losartan has a specific uricosuric action and may be particularly suitable for the many patients who have coexistent hypertension

calcium channel blockers also increase uric acid levels, possibly by a renal vasodilatory effect

increased vitamin C intake (either supplements or through normal diet) may also decrease serum uric acid levels

A 25-year-old woman presents with a three day history of dysuria and a painful left knee. During the review of symptoms she mentions a bout of diarrhoea and crampy abdominal pain three weeks ago. She is normally fit and well and takes no regular medication. Her father died of colorectal cancer in his sixth decade. On examination the left knee is red, swollen and hot to touch. What is the most likely diagnosis?

☐	Reactive arthritis secondary to <i>Salmonella</i> spp.
☐	Reactive arthritis secondary to <i>Chlamydia trachomatis</i>
☐	Rheumatoid arthritis
☐	Ulcerative colitis
☐	Gonococcal arthritis

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Submit answer

rethritis + arthritis + conjunctivitis = reactive arthritis

Two of the classic three features of reactive arthritis (urethritis, arthritis and conjunctivitis) are present in this patient. The family history of colorectal cancer is of no particular significance. Symptoms of reactive arthritis typically appear 1-4 weeks following the initial infection, in this case a diarrhoeal illness.

Reactive arthritis

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

Epidemiology

- post-STI form much more common in men (e.g. 10:1)
- post-dysenteric form equal sex incidence

The table below shows the organisms that are most commonly associated with reactive arthritis:

Post-dysenteric form	Post-STI form
<i>Shigella flexneri</i> <i>Salmonella typhimurium</i> <i>Salmonella enteritidis</i> <i>Yersinia enterocolitica</i> <i>Campylobacter</i>	<i>Chlamydia trachomatis</i>

Management

- symptomatic: analgesia, NSAIDS, intra-articular steroids
- sulfasalazine and methotrexate are sometimes used for persistent disease
- symptoms rarely last more than 12 months

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An autoantibody screen reveals that a patient is positive for anti-Jo 1 antibodies. What is the most likely underlying diagnosis?

☐	Limited cutaneous systemic sclerosis
☐	Mixed connective tissue disease
☐	Dermatomyositis
☐	Polymyositis
☐	Diffuse cutaneous systemic sclerosis

Submit answer

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د. حاصی وراز ©

Anti-Jo 1 antibodies are more commonly seen in polymyositis than dermatomyositis

Extractable nuclear antigens

Overview

- specific nuclear antigens
- usually associated with being ANA positive

Examples

- anti-Ro: Sjogren's syndrome, SLE, congenital heart block
- anti-La: Sjogren's syndrome
- anti-Jo 1: polymyositis
- anti-scl-70: diffuse cutaneous systemic sclerosis
- anti-centromere: limited cutaneous systemic sclerosis

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A 72-year-old woman is reviewed in the osteoporosis clinic. She had a hip fracture 5 years ago after which she was started on alendronate. This had to be stopped due to persistent musculoskeletal pain. Risedronate also had to be stopped for similar reasons. Strontium ranelate was therefore started but this was stopped following the development of a deep vein thrombosis. Her current T-score is -4.1. It has therefore been decided to start a trial of denosumab. What is the mechanism of action of this drug?

☐	Monoclonal antibody against osteoprotegerin
☐	Selective oestrogen receptor modulator
☐	Inhibits RANK ligand, which in turn inhibits the maturation of osteoclasts
☐	Promotes differentiation of pre-osteoblasts to osteoblasts + inhibits osteoclasts
☐	Pyrophosphate analog which inhibits osteoclast activity

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Osteoporosis: secondary prevention

NICE guidelines were updated in 2008 on the secondary prevention of osteoporotic fractures in postmenopausal women.

Key points include

- treatment is indicated following osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (a T-score of -2.5 SD or below). In women aged 75 years or older, a DEXA scan may not be required 'if the responsible clinician considers it to be clinically inappropriate or unfeasible'
- vitamin D and calcium supplementation should be offered to all women unless the clinician is confident they have adequate calcium intake and are vitamin D replete
- alendronate is first-line
- around 25% of patients cannot tolerate alendronate, usually due to upper gastrointestinal problems. These patients should be offered risidronate or etidronate (see treatment criteria below)
- strontium ranelate and raloxifene are recommended if patients cannot tolerate bisphosphonates (see treatment criteria below)

Treatment criteria for patients not taking alendronate

Unfortunately, a number of complicated treatment cut-off tables have been produced in the latest guidelines for patients who do not tolerate alendronate

These take into account a patient's age, their T-score and the number of risk factors they have from the following list:

- parental history of hip fracture
- alcohol intake of 4 or more units per day
- rheumatoid arthritis

It is very unlikely that examiners would expect you to have memorised these risk tables so we've not included them in the revision notes but they may be found by following the NICE link. The most important thing to remember is:

- the T-score criteria for risidronate or etidronate are less than the others implying that these are the second line drugs
- if alendronate, risidronate or etidronate cannot be taken then strontium ranelate or raloxifene may be given based on quite strict T-scores (e.g. a 60-year-old woman would need a T-score < -3.5)
- the strictest criteria are for denosumab

Supplementary notes on treatment

Bisphosphonates

- alendronate, risidronate and etidronate are all licensed for the prevention and treatment of post-menopausal and glucocorticoid-induced osteoporosis
- all three have been shown to reduce the risk of both vertebral and non-vertebral fractures although alendronate, risidronate may be superior to etidronate in preventing hip fractures
- ibandronate is a once-monthly oral bisphosphonate

Vitamin D and calcium

- poor evidence base to suggest reduced fracture rates in the general population at risk of osteoporotic fractures - may reduce rates in frail, housebound patients

Raloxifene - selective oestrogen receptor modulator (SERM)

- has been shown to prevent bone loss and to reduce the risk of vertebral fractures, but has not yet been shown to reduce the risk of non-vertebral fractures
- has been shown to increase bone density in the spine and proximal femur
- may worsen menopausal symptoms
- increased risk of thromboembolic events
- may decrease risk of breast cancer

Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts (promotes differentiation of pre-osteoblast to osteoblast) and reduces the resorption of bone by inhibiting osteoclasts
- strong evidence base, may be second-line treatment in near future
- increased risk of thromboembolic events

Denosumab

- human monoclonal antibody that inhibits RANK ligand, which in turn inhibits the maturation of osteoclasts
- given as a single subcutaneous injection every 6 months
- initial trial data suggests that it is effective and well tolerated

Teriparatide

- recombinant form of parathyroid hormone
- very effective at increasing bone mineral density but role in the management of osteoporosis yet to be clearly defined

Hormone replacement therapy

- has been shown to reduce the incidence of vertebral fracture and non-vertebral fractures
- due to concerns about increased rates of cardiovascular disease and breast cancer it is no longer recommended for primary or secondary prevention of osteoporosis unless the woman is suffering from vasomotor symptoms

Hip protectors

- evidence to suggest significantly reduce hip fractures in nursing home patients
- compliance is a problem

Falls risk assessment

- no evidence to suggest reduced fracture rates
- however, do reduce rate of falls and should be considered in management of high risk patients

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Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts (promotes differentiation of pre-osteoblast to osteoblast) and reduces the resorption of bone by inhibiting osteoclasts
- concerns regarding the safety profile of strontium have been raised recently. It should only be prescribed by a specialist in secondary care
- due to these concerns the European Medicines Agency in 2014 said it should only be used by people for whom there are no other treatments for osteoporosis
- increased risk of cardiovascular events: any history of cardiovascular disease or significant risk of cardiovascular disease is a contraindication
- increased risk of thromboembolic events: a Drug Safety Update in 2012 recommended it is not used in patients with a history of venous thromboembolism
- may cause serious skin reactions such as Stevens Johnson syndrome

Which one of the following is least recognised as a risk factor for developing osteoporosis?

☐	Cushing's syndrome
☐	Turner's syndrome
☐	Hyperparathyroidism
☐	Hypothyroidism
☐	Diabetes mellitus

Submit answer

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☒	Hypothyroidism
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Submit answer

Hyperthyroidism is associated with an increased risk of osteoporosis. Patients with hypothyroidism who take excessive amounts of levothyroxine may also be at risk of osteoporosis

Osteoporosis: causes

Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

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A 43-year-old woman presents with right-sided elbow pain. This has been present for the past month and she reports no obvious trigger. On examination she reports pain when the wrist is extended whilst the elbow is extended. What is the most likely diagnosis?

☐	Cubital tunnel syndrome
☐	Lateral epicondylitis
☐	Carpal tunnel syndrome
☐	Medial epicondylitis
☐	Pronator syndrome

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Submit answer

Lateral epicondylitis

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

Features

- pain and tenderness localised to the lateral epicondyle
- pain worse on wrist extension against resistance with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

Management options

- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy

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A 57-year-old man presents with pain in his right knee. An x-ray shows osteoarthritis. He has no past medical history of note. What is the most suitable treatment option for the management of his pain?

☐	Oral diclofenac with omeprazole
☐	Oral glucosamine
☐	Oral diclofenac
☐	Oral ibuprofen
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Submit answer

Osteoarthritis - paracetamol + topical NSAIDs (if knee/hand) first-line

Oral NSAIDs should be used second line in osteoarthritis due to their adverse effect profile

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

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A 31-year-old woman presents as her fingers intermittently turn white and become painful. She describes the fingers first turning white, then blue and finally red. This is generally worse in the winter months but it is present all year round. Wearing gloves does not help. Clinical examination of her hands, other joints and skin is unremarkable. Which one of the following treatments may be beneficial?

☐	Amitriptyline
☐	Aspirin
☐	Pregabalin
☐	Propranolol
☐	Nifedipine

Submit answer

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☐	Aspirin
☐	Pregabalin
☐	Propranolol
☒	Nifedipine

Submit answer

This lady has Raynaud's disease.

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

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A 79-year-old man presents with a history of lower back pain and right hip pain. Blood tests reveal the following:

Calcium	2.20 mmol/l
Phosphate	0.8 mmol/l
ALP	890 u/L

What is the most likely diagnosis?

☐	Primary hyperparathyroidism
☐	Chronic kidney disease
☐	Osteomalacia
☐	Osteoporosis
☐	Paget's disease

Submit answer

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Submit answer

The normal calcium and phosphate combined with a raised alkaline phosphate points to a diagnosis of Paget's

Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

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A 25-year-old man presents with back pain. Which one of the following may suggest a diagnosis of ankylosing spondylitis?

☐	Rapid onset
☐	Gets worse following exercise
☐	Bone tenderness
☐	Pain at night
☐	Improves with rest

Submit answer

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Submit answer

Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

<http://www.arthritisresearchuk.org/arthritis-information/conditions/ankylosing-spondylitis.aspx>

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Perinuclear antineutrophil cytoplasmic antibodies (pANCA) are most strongly associated with which condition?

- | | |
|-----------------------|--------------------------|
| ☐ | Goodpasture's syndrome |
| ☐ | Churg-Strauss syndrome |
| ☐ | Polyarteritis nodosa |
| ☐ | Wegener's granulomatosis |
| ☐ | Autoimmune hepatitis |

Submit answer

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| ☐ | Wegener's granulomatosis |
| ☐ | Autoimmune hepatitis |

Submit answer

ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:

- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

cANCA

- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

pANCA

- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- primary sclerosing cholangitis, positive in 60-80%
- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)

- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

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The presence of anti-cyclic citrullinated peptide antibody is suggestive of which one of the following conditions?

☐	Systemic lupus erythematosus
☐	Rheumatoid arthritis
☐	Type 1 diabetes mellitus
☐	Addison's disease
☐	Dermatomyositis

Submit answer

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Submit answer

Anti-cyclic citrullinated peptide antibody may be detectable up to 10 years before the development of rheumatoid arthritis. It may therefore play a key role in the future of rheumatoid arthritis, allowing early detection of patients suitable for aggressive anti-TNF therapy. It has a sensitivity similar to rheumatoid factor (70-80%, see below) with a much higher specificity of 90-95%.

Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

A 27-year-old woman presents with painful genital ulceration. She has had recurrent attacks for the past four years. Oral aciclovir has had little effect on the duration of her symptoms. She has also noticed for the past year almost weekly attacks of mouth ulcers which again are slow to heal. Her only past medical history of note is being treated for thrombophlebitis two years ago. What is the most likely diagnosis?

☐	Behcet's syndrome
☐	Polyarteritis nodosa
☐	Systemic lupus erythematosus
☐	Sarcoidosis
☐	Herpes simplex virus type 2

Submit answer

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Behcet's syndrome

Behcet's syndrome is a complex multisystem disorder associated with presumed autoimmune mediated inflammation of the arteries and veins. The precise aetiology has yet to be elucidated however. The classic triad of symptoms are oral ulcers, genital ulcers and anterior uveitis

Epidemiology

- more common in the eastern Mediterranean (e.g. Turkey)
- more common in men (complicated gender distribution which varies according to country. Overall, Behcet's is considered to be more common and more severe in men)
- tends to affect young adults (e.g. 20 - 40 years old)
- associated with HLA B5* and MICA6 allele
- around 30% of patients have a positive family history

Features

- classically: 1) oral ulcers 2) genital ulcers 3) anterior uveitis
- thrombophlebitis
- arthritis
- neurological involvement (e.g. aseptic meningitis)
- GI: abdo pain, diarrhoea, colitis
- erythema nodosum, DVT

Diagnosis

- no definitive test
- diagnosis based on clinical findings
- positive pathergy test is suggestive (puncture site following needle prick becomes inflamed with small pustule forming)

*more specifically HLA B51, a split antigen of HLA B5

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Which one of the following statements regarding the 2010 American College of Rheumatology / European League Against Rheumatism classification criteria for rheumatoid arthritis is correct?

☐	A score of 7 out of 10 is sufficient to diagnose definite rheumatoid arthritis
☐	Inflammatory markers such as CRP and ESR are not part of the diagnostic criteria
☐	Patients must have either a positive rheumatoid factor or a positive anti-cyclic citrullinated peptide antibody
☐	Large joint arthritis is more relevant than small joint arthritis
☐	Gender is part of the scoring system

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Submit answer

Rheumatoid arthritis: diagnosis

NICE have stated that clinical diagnosis is more important than criteria such as those defined by the American College of Rheumatology.

2010 American College of Rheumatology criteria

Target population. Patients who

- 1) have at least 1 joint with definite clinical synovitis
- 2) with the synovitis not better explained by another disease

Classification criteria for rheumatoid arthritis (add score of categories A-D; a score of 6/10 is needed definite rheumatoid arthritis)

Key

- RF = rheumatoid factor
- ACPA = anti-cyclic citrullinated peptide antibody

Factor	Scoring	
A. Joint involvement		
	1 large joint	0
	2 - 10 large joints	1
	1 - 3 small joints (with or without involvement of large joints)	2
	4 - 10 small joints (with or without involvement of large joints)	3
	10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification)		
	Negative RF and negative ACPA	0
	Low-positive RF or low-positive ACPA	2
	High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)		
	Normal CRP and normal ESR	0
	Abnormal CRP or abnormal ESR	1
D. Duration of symptoms		
	< 6 weeks	0
	> 6 weeks	1

http://www.rheumatology.org/Portals/0/Files/2010_revised_criteria_classification_ra.pdf

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A 56-year-old lady is referred to rheumatology clinic due to severe Raynaud's phenomenon associated with arthralgia of the fingers. On examination you note shiny and tight skin of the fingers with a number of telangiectasia on the upper torso and face. She is also currently awaiting a gastroscopy to investigate heartburn. Which one of the following antibodies is most specific for the underlying condition?

☐	Anti-Jo 1 antibodies
☐	Rheumatoid factor
☐	Anti-Scl-70 antibodies
☐	Anti-centromere antibodies
☐	Anti-nuclear factor

Submit answer

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☒	Anti-centromere antibodies
☐	Anti-nuclear factor

Submit answer

This lady has some features of CREST syndrome. Although ANA is positive in 90% of patients with systemic sclerosis, anti-centromere antibodies are the most specific test for limited cutaneous systemic sclerosis

Limited (central) systemic sclerosis = anti-centromere antibodies

Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear



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Antibodies

- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

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Which one of the following is true regarding the investigation of a patient with dermatomyositis?

☐	Creatine kinase is characteristically normal
☐	Muscle biopsy is contraindicated
☐	Anti-Jo-1 antibodies are usually negative
☐	Antinuclear antibodies are always negative
☐	EMG is normal

Submit answer

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☐	EMG is normal

Submit answer

Anti-Jo-1 antibodies are more common in polymyositis than dermatomyositis

Dermatomyositis: investigations and management

Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever

Management

- prednisolone

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Which one of the following statements concerning discoid lupus is correct?

☐	Commonly progresses to SLE
☐	Causes non-scarring alopecia
☐	Characterised by follicular keratin plugs
☐	Is rarely photosensitive
☐	Typically presents in older males

Submit answer

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Submit answer

Discoid lupus erythematosus is characterised by follicular keratin plugs

Discoid lupus erythematosus

Discoid lupus erythematosus is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematosus is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

Features

- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

Management

- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure



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Discoid lupus erythematosus affecting the scalp

A 31-year-old female with a history of SLE gives birth following a 39 week pregnancy. The newborn is noted to be bradycardic. Which one of the following autoantibodies are associated with congenital heart block?

☐	Anti-Ro
☐	Anti-Sm
☐	Anti-RNP
☐	Anti-dsDNA
☐	Anti-Jo 1

Submit answer

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☐	Anti-dsDNA
☐	Anti-Jo 1

Submit answer

SLE: pregnancy

Overview

- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematosus
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies

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A 45-year-old woman with a history of primary Sjogren's syndrome is reviewed in clinic. Her main problem is a dry mouth, which unfortunately has not responded to artificial saliva. Which one of the following medications is most likely to be beneficial?

☐	Rivastigmine
☐	Neostigmine
☐	Clonidine
☐	Atropine
☐	Pilocarpine

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Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management

- artificial saliva and tears
- pilocarpine may stimulate saliva production

A 45-year-old woman is referred to rheumatology outpatients with a 4 month history of joint pains, myalgia and generalised lethargy. An autoantibody screen reveals she is ANA positive and anti-ribonucleoprotein positive. The creatine kinase is elevated at 525. What is the most likely diagnosis?

☐	Systemic lupus erythematosus
☐	Mixed connective tissue disease
☐	Polymyositis
☐	Dermatomyositis
☐	CREST syndrome

Submit answer

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☐	Dermatomyositis
☐	CREST syndrome

Submit answer

Mixed connective tissue disease

Features of SLE, systemic sclerosis and polymyositis

Anti-RNP positive

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A 57-year-old man with a history of ischaemic heart disease presents with an hot, erythematous and painful left 1st metatarsophalangeal joint. The attack settles following a course of non-steroidal anti-inflammatories. He currently takes aspirin 75 mg od for secondary prevention of ischaemic heart disease. What should happen regarding his medication?

☐	Switch aspirin to clopidogrel
☐	Continue aspirin at current dose
☐	Increase aspirin dose to 300mg od
☐	Switch aspirin to dipyridamole
☐	Stop aspirin

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Submit answer

Aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - please see the British Society for Rheumatology guidelines for more details.

Gout: drug causes

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Drug causes

- thiazides, furosemide
- alcohol
- cytotoxic agents
- pyrazinamide

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Osteopetrosis is due to a defect in:

☐	Osteoclast function
☐	PTH receptors
☐	Osteoblast function
☐	Calcium resorption in proximal tubule
☐	Calcium absorption

Submit answer

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Osteopetrosis

Overview

- also known as marble bone disease
- rare disorder of defective osteoclast function resulting in failure of normal bone resorption
- results in dense, thick bones that are prone to fracture
- bone pains and neuropathies are common.
- calcium, phosphate and ALP are normal
- stem cell transplant and interferon-gamma have been used for treatment

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Each one of the following is seen in reactive arthritis, except:

☐	Urethritis
☐	Keratoderma blenorrhagica
☐	Conjunctivitis
☐	Aseptic meningoencephalitis
☐	Circinate balanitis

Submit answer

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Submit answer

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Reactive arthritis: features

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

Features

- typically develops within 4 weeks of initial infection - symptoms generally last around 4-6 months
- arthritis is typically an asymmetrical oligoarthritis of lower limbs
- dactylitis
- **symptoms of urethritis**
- eye: conjunctivitis (seen in 50%), anterior uveitis
- skin: circinate balanitis (painless vesicles on the coronal margin of the prepuce), keratoderma blenorrhagica (waxy yellow/brown papules on palms and soles)

Around 25% of patients have recurrent episodes whilst 10% of patients develop chronic disease



Keratoderma blenorrhagica

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Which of the following is not a recognised cause of Raynaud's phenomenon?

☐	Oral contraceptive pill
☐	Cervical rib
☐	Type I cryoglobulinaemia
☐	Pizotifen
☐	Scleroderma

Submit answer

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Ergotamine rather than pizotifen is associated with Raynaud's phenomenon

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

A 54-year-old man with a history of type 2 diabetes mellitus presents with a history of right shoulder pain. On examination there is limited movement of the right shoulder in all directions. What is the most likely diagnosis?

☐	Adhesive capsulitis
☐	Dermatomyositis
☐	Avascular necrosis
☐	Lhermitte's syndrome
☐	Diabetic amyotrophy

Submit answer

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Submit answer

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Diabetic amyotrophy affects the lower limbs

Adhesive capsulitis

Adhesive capsulitis (frozen shoulder) is a common cause of shoulder pain. It is most common in middle-aged patients. The aetiology of frozen shoulder is not fully understood.

Associations

- diabetes mellitus: up to 20% of diabetics may have an episode of frozen shoulder

Features

- external rotation is affected more than internal rotation or abduction
- both active and passive movement are affected
- patients typically have a painful freezing phase, an adhesive phase and a recovery phase
- bilateral in up to 20% of patients
- the episode typically lasts between 6 months and 2 years

Management

- no single intervention has been shown to improve outcome in the long-term
- treatment options include NSAIDs, physiotherapy, oral corticosteroids and intra-articular corticosteroids

A 54-year-old woman who has had two Colle's fractures in the past three years has a DEXA scan:

	T-score
L2-4	-1.4
Femoral neck	-2.7

What does the scan show?

☐	Osteoporosis in both the vertebrae and femoral neck
☐	Osteoporosis in vertebrae, osteopaenia in femoral neck
☐	Osteopaenia in both the vertebrae and femoral neck
☐	Osteopaenia in vertebrae, osteoporosis in femoral neck
☐	Normal bone density in vertebrae, osteoporosis in femoral neck

Submit answer

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Submit answer

Osteoporosis: DEXA scan

Basics

- T score: based on bone mass of young reference population
- T score of -1.0 means bone mass of one standard deviation below that of young reference population
- Z score is adjusted for age, gender and ethnic factors

T score

- > -1.0 = normal
- -1.0 to -2.5 = osteopaenia
- < -2.5 = osteoporosis

An 28-year-old man is investigated for recurrent lower back pain. A diagnosis of ankylosing spondylitis is suspected. Which one of the following investigations is most useful?

☐	ESR
☐	X-ray of the sacro-iliac joints
☐	HLA-B27 testing
☐	X-ray of the thoracic spine
☐	CT of the lumbar spine

Submit answer

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☐	CT of the lumbar spine

Submit answer

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X-ray of the sacro-iliac joints is the most useful investigation for diagnosis and monitoring, but changes may not be seen for many years after the onset of symptoms

Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 3:1) aged 20-30 years old.

Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis. Radiographs may be normal early in disease, later changes include:

- sacroiliitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- syndesmophytes: due to ossification of outer fibers of annulus fibrosus
- chest x-ray: apical fibrosis



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40-year-old male. There is typical appearance of bamboo spine with a single central radiodense line related to ossification of supraspinous and interspinous ligaments which is called dagger sign. Ankylosing is detectable in both sacroiliac joints



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Ankylosing spondylitis with well formed syndesmophytes



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Lateral cervical spine. Complete fusion of anterior and posterior elements in ankylosing spondylitis, so called bamboo spine



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Fusion of bilateral sacroiliac joints. Sacroiliitis may present as sclerosis of joint margins which can be asymmetrical at early stage of disease, but is bilateral and symmetrical in late disease



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Syndesmophytes and squaring of vertebral bodies. Squaring of anterior vertebral margins is due to osteitis of anterior corners. Syndesmophytes are due to ossification of outer fibers of annulus fibrosus

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

Management

The following is partly based on the 2010 EULAR guidelines (please see the link for more details):

- encourage regular exercise such as swimming
- physiotherapy
- NSAIDs are the first-line treatment
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- the 2010 EULAR guidelines suggest: *'Anti-TNF therapy should be given to patients with persistently high disease activity despite conventional treatments'*
- research is ongoing to see whether anti-TNF therapies such as etanercept and adalimumab should be used earlier in the course of the disease

Enter your notes here

Save my notes

Which one of the following conditions is least associated with HLA-B27?

☐	Reiter's syndrome
☐	Psoriatic arthritis
☐	Ankylosing spondylitis
☐	Crohn's disease
☐	Sacroiliitis

Submit answer

د. عاصم وراز ©

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☒	Crohn's disease
☐	Sacroiliitis

Submit answer

د. عاصم وراز ©

There is an indirect association between HLA-B27 and Crohn's as some patients may develop enteropathic arthritis, but this is the least common association of the above

Seronegative spondyloarthropathies

Common features

- associated with HLA-B27
- rheumatoid factor negative - hence 'seronegative'
- peripheral arthritis, usually asymmetrical
- sacroiliitis
- enthesopathy: e.g. Achilles tendonitis, plantar fasciitis
- extra-articular manifestations: uveitis, pulmonary fibrosis (upper zone), amyloidosis, aortic regurgitation

Spondyloarthropathies

- ankylosing spondylitis
- psoriatic arthritis
- Reiter's syndrome (including reactive arthritis)
- enteropathic arthritis (associated with IBD)

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You are doing the annual review of a 50-year-old woman who has rheumatoid arthritis. Which one of the following complications is most likely to occur as a result of her disease?

☐	Chronic lymphocytic leukaemia
☐	Hypertension
☐	Colorectal cancer
☐	Type 2 diabetes mellitus
☐	Ischaemic heart disease

Submit answer

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Submit answer

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Rheumatoid arthritis: complications

A wide variety of extra-articular complications occur in patients with rheumatoid arthritis (RA):

- respiratory: pulmonary fibrosis, pleural effusion, pulmonary nodules, bronchiolitis obliterans, methotrexate pneumonitis, pleurisy
- ocular: keratoconjunctivitis sicca (most common), episcleritis, scleritis, corneal ulceration, keratitis, steroid-induced cataracts, chloroquine retinopathy
- osteoporosis
- ischaemic heart disease: RA carries a similar risk to type 2 diabetes mellitus
- increased risk of infections
- depression

Less common

- Felty's syndrome (RA + splenomegaly + low white cell count)
- amyloidosis

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A 54-year-old male presents with weakness of his upper arms. On examination he is found to have a macular rash over his back and the extensor aspects of his upper arms. He is a heavy smoker and his sodium is 121 mmol/l. What is the most likely underlying diagnosis?

☐	Addison's disease
☐	Polymyositis
☐	Overlap syndrome
☐	Dermatomyositis
☐	Hypothyroidism

Submit answer

د. حاصیہ وراز ©

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☐	syndrome
☒	Dermatomyositis
☐	Hypothyroidism

Submit answer

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This man may have an underlying small cell lung cancer causing Syndrome of Inappropriate Antidiuretic Hormone Secretion.

Dermatomyositis

Overview

- inflammatory disorder causing symmetrical, proximal muscle weakness and characteristic skin lesions
- may be idiopathic or associated with connective tissue disorders or underlying malignancy (typically lung cancer, found in 20-25% - more if patient older)
- polymyositis is a variant of the disease where skin manifestations are not prominent

Skin features

- photosensitive
- macular rash over back and shoulder
- heliotrope rash in the periorbital region
- Gottron's papules - roughened red papules over extensor surfaces of fingers
- nail fold capillary dilatation

Other features

- proximal muscle weakness +/- tenderness
- Raynaud's
- respiratory muscle weakness
- interstitial lung disease: e.g. Fibrosing alveolitis or organising pneumonia
- dysphagia, dysphonia

Which of the following findings is not typical in a patient with antiphospholipid syndrome?

☐	Prolonged APTT
☐	Thrombocytosis
☐	Recurrent venous thrombosis
☐	Recurrent arterial thrombosis
☐	Livedo reticularis

Submit answer

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Submit answer

د. عاصم وراز ©

Thrombocytopenia is associated with antiphospholipid syndrome

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

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Which one of the following is least recognised as a risk factor for developing osteoporosis?

☐	Multiple myeloma
☐	Rheumatoid arthritis
☐	Long-term phenytoin therapy
☐	Chronic renal failure
☐	Diabetes mellitus

Submit answer

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Submit answer

د. عاصم وراز ©

Long-term phenytoin therapy may cause enhanced vitamin D metabolism leading to osteomalacia, rather than osteoporosis

Osteoporosis: causes

Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

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Save my notes

A 55-year-old woman presents with a four week history of shoulder pain. There has been no obvious precipitating injury and no previous experience. The pain is worse on movement and there is a grating sensation if she moves the arm too quickly. She also gets pain at night, particularly when she lies on the affected shoulder. On examination there is no obvious erythema or swelling. Passive abduction is painful between between 60 and 120 degrees. She is unable to abduct the arm herself past 70-80 degrees. Flexion and extension are preserved. What is the most likely diagnosis?

☐	Adhesive capsulitis (frozen shoulder)
☐	Supraspinatus tendonitis
☐	Acromioclavicular joint injury
☐	Glenohumeral arthritis
☐	Superior labral lesion

Submit answer

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Submit answer

This patient has a classic 'painful arc' which is a sign of shoulder impingement, most commonly secondary to supraspinatus tendonitis.

Rotator cuff muscles

SITS - small t for teres minor

Supraspinatus

Infraspinatus

teres minor

Subscapularis

Muscle	Notes
Supraspinatus	aBDucts arm before deltoid Most commonly injured
Infraspinatus	Rotates arm laterally
teres minor	aDDucts & rotates arm laterally
Subscapularis	aDDuct & rotates arm medially

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Save my notes

Which one of the following is least recognised in polyarteritis nodosa?

☐	Cytoplasmic-antineutrophil cytoplasmic antibodies
☐	Hypertension
☐	Mononeuritis multiplex
☐	Pyrexia
☐	Renal failure

Submit answer

د. عاصم وراز ©

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Submit answer

د. حاصیہ وراز ©

Perinuclear-antineutrophil cytoplasmic antibodies are found in around 20% of patients

Polyarteritis nodosa

Polyarteritis nodosa (PAN) is a vasculitis affecting medium-sized arteries with necrotizing inflammation leading to aneurysm formation. PAN is more common in middle-aged men and is associated with hepatitis B infection

Features

- fever, malaise, arthralgia
- weight loss
- hypertension
- mononeuritis multiplex, sensorimotor polyneuropathy
- testicular pain
- livedo reticularis
- haematuria, renal failure
- perinuclear-antineutrophil cytoplasmic antibodies (ANCA) are found in around 20% of patients with 'classic' PAN
- hepatitis B serology positive in 30% of patients



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Livedo reticularis

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A 51-year-old male presents with an acute onset of swelling and pain in his right knee. Aspiration shows negatively birefringent crystals with no organisms seen. His pain fails to settle with NSAIDs. What is the most appropriate next step in his management?

☐	Repeat joint aspiration and intra-articular depomededone
☐	Allopurinol
☐	IV flucloxacillin
☐	Diuretics
☐	Low dose methotrexate

Submit answer

د. عاصم وراز ©

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Submit answer

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Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid $> 450 \mu\text{mol/l}$)

Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine* has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of $< 300 \mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol**

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

Enter your notes here...

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Which of the following is least likely to be associated with ankylosing spondylitis?

☐	Apical fibrosis
☐	Achilles tendonitis
☐	Amyloidosis
☐	Achalasia
☐	Heart block

Submit answer

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Submit answer

د. حاصیہ وراز ©

Ankylosing spondylitis features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis

Achalasia is not a recognised association of ankylosing spondylitis

Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

Enter your notes here....

Save my notes

A 54-year-old man presents to the Emergency Department with a 2 day history of an swollen, painful left knee. Aspirated joint fluid shows calcium pyrophosphate crystals. Which of the following blood tests is most useful in revealing an underlying cause?

☐	Transferrin saturation
☐	ACTH
☐	ANA
☐	Serum ferritin
☐	LDH

Submit answer

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Submit answer

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This is a typical presentation of pseudogout. An elevated transferrin saturation may indicate haemochromatosis, a recognised cause of pseudogout

A high ferritin level is also seen in haemochromatosis but can be raised in a variety of infective and inflammatory processes, including pseudogout, as part of an acute phase response

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

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A 40-year-old woman complains of a permanent 'funny-bone' sensation in her right elbow. This is accompanied by tingling in the little and ring finger. Her symptoms are worse when the elbow is bent for prolonged periods. What is the most likely diagnosis?

☐	Cubital tunnel syndrome
☐	Lateral epicondylitis
☐	Medial epicondylitis
☐	Median nerve entrapment syndrome
☐	Radial tunnel syndrome

Submit answer

د. حاصم دراز ©

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Submit answer

د. جاسم دراز ©

Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

Lateral epicondylitis (tennis elbow)	Features • pain and tenderness localised to the lateral epicondyle • pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended • episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks
Medial epicondylitis (golfer's elbow)	Features • pain and tenderness localised to the medial epicondyle • pain is aggravated by wrist flexion and pronation • symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement
Radial tunnel syndrome	Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse. Features • symptoms are similar to lateral epicondylitis making it difficult to diagnose • however, the pain tends to be around 4-5 cm distal to the lateral epicondyle • symptoms may be worsened by extending the elbow and pronating the forearm
Cubital tunnel syndrome	Due to the compression of the ulnar nerve. Features • initially intermittent tingling in the 4th and 5th finger • may be worse when the elbow is resting on a firm surface or flexed for extended periods • later numbness in the 4th and 5th finger with associated weakness
Olecranon bursitis	Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.

A 41-year-old man presents with persistent fatigue for the past 8 months. Which one of the following features is least consistent with a diagnosis of chronic fatigue syndrome?

☐	Dizziness
☐	Painful lymph nodes without enlargement
☐	Having a busy day improves the symptoms
☐	Palpitations
☐	Headaches

Submit answer

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☐	Palpitations
☐	Headaches

Submit answer

د. حاصی وراز ©

Physical or mental exertion usually makes the symptoms worse

Chronic fatigue syndrome

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

Epidemiology

- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include

- sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep-wake cycle
- muscle and/or joint pains
- headaches
- painful lymph nodes without enlargement
- sore throat
- cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
- physical or mental exertion makes symptoms worse
- general malaise or 'flu-like' symptoms
- dizziness
- nausea
- palpitations

Investigation

- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin*, coeliac screening and also urinalysis

Management

- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

*children and young people only

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Which one of the following is least associated with Behcet's syndrome?

☐	Mouth ulcers
☐	Genital ulcers
☐	Conjunctivitis
☐	Deep vein thrombosis
☐	Aseptic meningitis

Submit answer

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Submit answer

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Mouth ulcers, genital ulcers, deep vein thrombosis and aseptic meningitis are all recognised features of Behcet's syndrome

Ocular involvement is the most feared complication of Behcet's syndrome. Conjunctivitis is seen rarely and is much less common than anterior uveitis. Other ocular problems seen include retinal vasculitis, iridocyclitis and chorioretinitis

Behcet's syndrome

Behcet's syndrome is a complex multisystem disorder associated with presumed autoimmune mediated inflammation of the arteries and veins. The precise aetiology has yet to be elucidated however. The classic triad of symptoms are oral ulcers, genital ulcers and anterior uveitis

Epidemiology

- more common in the eastern Mediterranean (e.g. Turkey)
- more common in men (complicated gender distribution which varies according to country. Overall, Behcet's is considered to be more common and more severe in men)
- tends to affect young adults (e.g. 20 - 40 years old)
- associated with HLA B5* and MICA6 allele
- around 30% of patients have a positive family history

Features

- classically: 1) oral ulcers 2) genital ulcers 3) anterior uveitis
- thrombophlebitis
- arthritis
- neurological involvement (e.g. aseptic meningitis)
- GI: abdo pain, diarrhoea, colitis
- erythema nodosum, DVT

Diagnosis

- no definitive test
- diagnosis based on clinical findings
- positive pathergy test is suggestive (puncture site following needle prick becomes inflamed with small pustule forming)

*more specifically HLA B51, a split antigen of HLA B5

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A 31-year-old patient is diagnosed with rheumatoid arthritis. Which of the following is associated with a good prognosis?

- | | |
|-----------------------|--|
| ☐ | Being a non-smoker |
| ☐ | Erosions on x-ray first developing 18 months after diagnosis |
| ☐ | Sudden onset |
| ☐ | Being diagnosed aged 35 years |
| ☐ | Anti-CCP antibodies |

Submit answer

د. عاصم وراز ©

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Submit answer

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Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

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A 44-year-old female with a history of Raynaud's phenomenon is reviewed in the rheumatology clinic. She is currently being investigated for dysphagia. On examination she is noted to have tight, shiny skin over her fingers. Which one of the following complications is she most likely to develop?

☐	Early onset dementia
☐	Erythema nodosum
☐	Malabsorption
☐	Constrictive pericarditis
☐	Erosive joint disease

Submit answer

د. عاصم وراز ©

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Submit answer

د. عاصم وراز ©

This patient is likely to have CREST syndrome, a subtype of limited cutaneous systemic sclerosis. Malabsorption can develop in these patients secondary to bacterial overgrowth of the sclerosed small intestine

Whilst diffuse systemic sclerosis is associated with more severe and rapid internal organ involvement it is also seen in the limited form.

Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear



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Antibodies

- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

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Which one of the following features is least typical of polymyalgia rheumatica?

☐	Elevated creatinine kinase
☐	Low-grade fever
☐	Morning stiffness in proximal limb muscles
☐	Polyarthralgia
☐	Anorexia

Submit answer

د. عاصم وراز ©

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Submit answer

د. عاصم وراز ©

Polymyalgia rheumatica

Pathophysiology

- overlaps with temporal arteritis
- histology shows vasculitis with giant cells, characteristically 'skips' certain sections of affected artery whilst damaging others
- muscle bed arteries affected most in polymyalgia rheumatica

Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- aching, morning stiffness in proximal limb muscles (not weakness)
- also mild polyarthralgia, lethargy, depression, low-grade fever, anorexia, night sweats

Investigations

- ESR > 40 mm/hr
- note CK and EMG normal
- reduced CD8+ T cells

Treatment

- prednisolone e.g. 15mg/od - dramatic response

http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/m/management_of_polymyalgia_rheumatica.pdf

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A 61-year-old man is noted to have thickened patches of skin over his knuckles and extensor surfaces consistent with Gottron's papules. His creatinine kinase levels are also elevated. A diagnosis of dermatomyositis is suspected. Which one of the following types of autoantibody is most specific for this condition?

☐	Anti-scl-70 antibodies
☐	Anti-Jo-1 antibodies
☐	Anti-nuclear antibodies
☐	Anti-Mi-2 antibodies
☐	Anti-centromere bodies

Submit answer

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Submit answer

Dermatomyositis antibodies: ANA most common, anti-Mi-2 most specific

Dermatomyositis: investigations and management

Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever

Management

- prednisolone

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Which one of the following statements regarding ankylosing spondylitis is correct?

- | | |
|-----------------------|--|
| ☐ | Schober's test assesses reduced chest expansion |
| ☐ | HLA-B27 is positive in 50% of patients |
| ☐ | Achilles tendonitis is a recognised association |
| ☐ | It affects men twice as commonly as women |
| ☐ | The typical age of presentation is between 40-50 years |

Submit answer

د. حاصیہ وراز ©

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Submit answer

د. جاسم وراز ©

HLA-B27 is positive in 90% of patients.

Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

Enter your notes here...

Save my notes

A 54-year-old man is recovering following his first episode of gout. The pain and inflammation settled 4 days ago. He has no risk factors for the development of gout and there is no evidence of gouty tophi on examination. What is the most suitable point to start uric acid lowering therapy?

☐	Immediately
☐	If more than 6 episodes of gout in a 1 year period
☐	If one further attack of gout in the next 12 months
☐	4 weeks after the initial attack of gout has settled
☐	If more than 4 episodes of gout in a 1 year period

Submit answer

د. حاصو وراز ©

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Submit answer

د. عاصم وراز ©

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid $> 450 \mu\text{mol/l}$)

Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine* has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of $< 300 \mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol**

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

Enter your notes here...

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Which one of the following conditions has polygenic inheritance?

- | | |
|-----------------------|--------------------------|
| ☐ | Bartter's syndrome |
| ☐ | Huntington disease |
| ☐ | Ankylosing spondylitis |
| ☐ | Fragile X syndrome |
| ☐ | Von Willebrand's disease |

Submit answer

د. عاصم دراز ©

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Huntington disease



Ankylosing spondylitis



Fragile X syndrome



Von Willebrand's disease

Submit answer

د. عاصم دراز ©

Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 3:1) aged 20-30 years old.

Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis.

Radiographs may be normal early in disease, later changes include:

- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- syndesmophytes: due to ossification of outer fibers of annulus fibrosus
- chest x-ray: apical fibrosis



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40-year-old male. There is typical appearance of bamboo spine with a single central radiodense line related to ossification of supraspinous and interspinous ligaments which is called dagger sign. Ankylosing is detectable in both sacroiliac joints.



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Ankylosing spondylitis with well formed syndesmophytes



© Image used on license from Radiopaedia

Lateral cervical spine. Complete fusion of anterior and posterior elements in ankylosing spondylitis, so called bamboo spine



© Image used on license from Radiopaedia

Fusion of bilateral sacroiliac joints. Sacroilitis may present as sclerosis of joint margins which can be asymmetrical at early stage of disease, but is bilateral and symmetrical in late disease



© Image used on license from Radiopaedia

Syndesmophytes and squaring of vertebral bodies. Squaring of anterior vertebral margins is due to osteitis of anterior corners. Syndesmophytes are due to ossification of outer fibers of annulus fibrosus

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

Management

The following is partly based on the 2010 EULAR guidelines (please see the link for more details):

- encourage regular exercise such as swimming
- physiotherapy
- NSAIDs are the first-line treatment
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- the 2010 EULAR guidelines suggest: 'Anti-TNF therapy should be given to patients with persistently high disease activity despite conventional treatments'
- research is ongoing to see whether anti-TNF therapies such as etanercept and adalimumab should be used earlier in the course of the disease

Enter your notes here ...

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د. ناصر وراز ©

A 47-year-old female presents with elbow pain. She has just spent the weekend painting the house. On examination there is localised pain around the lateral epicondyle and a diagnosis of lateral epicondylitis is suspected. Which one of the following movements would characteristically worsen the pain?

☐	Resisted thumb flexion
☐	Thumb extension
☐	Flexion of the elbow
☐	Pronation of the forearm with the elbow flexed
☐	Resisted wrist extension with the elbow extended

Submit answer

د. حاصی وراز ©

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☒	Resisted wrist extension with the elbow extended

Submit answer

د. حاصیہ وراز

Lateral epicondylitis: worse on resisted wrist extension/supination whilst elbow extended

Lateral epicondylitis

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

Features

- pain and tenderness localised to the lateral epicondyle
- pain worse on wrist extension against resistance with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

Management options

- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy

Enter your notes here...

Save my notes

Approximately what percentage of patients with psoriasis develop an associated arthropathy?

☐	0.5%
☐	12-15%
☐	4-5%
☐	1%
☐	10%

Submit answer

د. عاصم وراز ©

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د. عاصم وراز ©

Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10% percent of patients with skin lesions develop an arthropathy with males and females being equally affected

Types*

- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management

- treat as rheumatoid arthritis
- but better prognosis

*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies

Enter your notes here...

Save my notes

You review a 48-year-old woman who is taking methotrexate for rheumatoid arthritis. Concurrent prescription of which other medication should be avoided?

- | | |
|-----------------------|------------------|
| ☐ | Erythromycin |
| ☐ | Trimethoprim |
| ☐ | Sumatriptan |
| ☐ | Lansoprazole |
| ☐ | Sodium valproate |

Submit answer

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Submit answer

د. عاصم وراز ©

There is an increased risk of haematological toxicity when trimethoprim is prescribed alongside methotrexate.

Methotrexate

Methotrexate is an antimetabolite which inhibits dihydrofolate reductase, an enzyme essential for the synthesis of purines and pyrimidines

Indications

- rheumatoid arthritis
- psoriasis
- acute lymphoblastic leukaemia

Adverse effects

- mucositis
- myelosuppression
- pneumonitis
- pulmonary fibrosis
- liver cirrhosis

Pregnancy

- women should avoid pregnancy for at least 3 months after treatment has stopped
- the BNF also advises that men using methotrexate need to use effective contraception for at least 3 months after treatment

Prescribing methotrexate

- methotrexate is a drug with a high potential for patient harm. It is therefore important that you are familiar with guidelines relating to its use
- methotrexate is taken weekly, rather than daily
- FBC, U&E and LFTs need to be regularly monitored. The Committee on Safety of Medicines recommend 'FBC and renal and LFTs before starting treatment and repeated weekly until therapy stabilised, thereafter patients should be monitored every 2-3 months'
- folic acid 5mg once weekly should be co-prescribed, taken more than 24 hours after methotrexate dose
- the starting dose of methotrexate is 7.5 mg weekly (source: BNF)
- only one strength of methotrexate tablet should be prescribed (usually 2.5 mg)
- avoid prescribing trimethoprim or cotrimoxazole concurrently - increases risk of marrow aplasia

A 68-year-old presents with a painful swollen left knee which has failed to settle after a weeks rest. There is no history of trauma. On examination he has a moderate sized effusion. A plain radiograph is reported as follows:

Some loss of joint space
Linear calcification of the articular cartilage

What is the most likely diagnosis?

☐	Pseudogout
☐	Rheumatoid arthritis
☐	Sarcoidosis
☐	Gout
☐	Osteoarthritis

Submit answer

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☐	Osteoarthritis

Submit answer

This x-ray describes chondrocalcinosis. Non-specific changes such as loss of joint space are common in this age group and pseudogout itself may cause osteoarthritic-like changes.

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

Enter your notes here...

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A 69-year-old man presents with an acute episode of gout on his left first metatarsal-phalangeal joint. What is the most likely underlying mechanism?

☐	Sedentary lifestyle
☐	Decreased renal excretion of uric acid
☐	Increased endogenous production of uric acid
☐	Starvation
☐	Too much protein in diet

Submit answer

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Submit answer

د. عاصم وراز ©

The vast majority of gout is due to decreased renal excretion of uric acid

Decreased renal excretion of uric acid is thought to account for 90% of cases of primary gout. Secondary risk factors such as alcohol intake and medications should also be investigated

Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid

- drugs*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid

- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome

- hypoxanthine-guanine phosphoribosyl transferase (HGPRTase) deficiency
- x-linked recessive
- features: gout, renal failure, neurological deficits, learning difficulties, self-mutilation

*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

A 50-year-old man with no past medical history is investigated for ongoing back pain. He is found to have a vertebral collapse secondary to osteoporosis. What is the most appropriate test to determine the cause of his osteoporosis?

☐	Thyroid function tests
☐	Prostate specific antigen
☐	Oestrogen level
☐	Prolactin level
☐	Testosterone level

Submit answer

د. حاصو وراز ©

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Submit answer

د. حاصو وراز ©

Whilst thyrotoxicosis is a known cause of osteoporosis, testosterone deficiency is much more likely in a middle-aged male

Osteoporosis: causes

Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

Enter your notes here...

Save my notes

A 54-year-old farm worker presents for review. She has recently been diagnosed with osteoarthritis of the hand but has no other past medical history of note. Despite regular paracetamol she is still experiencing considerable pain, especially around the base of both thumbs. What is the most suitable next management step?

- | | |
|-----------------------|---|
| ☐ | Add oral diclofenac + lansoprazole |
| ☐ | Switch paracetamol for co-codamol 8/500 |
| ☐ | Add topical ibuprofen |
| ☐ | Add oral ibuprofen |
| ☐ | Add oral glucosamine |

Submit answer

د. عاصم دراز ©

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Submit answer

The 2008 NICE guidelines suggest the use of paracetamol and topical NSAIDs first-line

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Enter your notes here...

Save my notes

A 24-year-old female is investigated for intermittent pain and swelling of the metacarpal phalangeal joints for the past 3 months. An x-ray shows loss of joint space and soft-tissue swelling. Rheumatoid factor is positive and a diagnosis of rheumatoid arthritis is made. What is the most appropriate management to slow disease progression?

☐	Infliximab
☐	Rituximab
☐	Sulfasalazine
☐	Methotrexate + sulfasalazine + short-course of prednisolone
☐	Diclofenac

Submit answer

د. حاصیہ وراز ©

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Submit answer

د. حاصی وراز ©

The 2009 NICE guidelines recommend that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids). Women of child-bearing age should be given effective contraception for the duration of treatment and for 3 months after methotrexate has been stopped.

Rheumatoid arthritis: management

The management of rheumatoid arthritis (RA) has been revolutionised by the introduction of disease-modifying therapies in the past decade. NICE has issued a number of technology appraisals on the newer agents and released general guidelines in 2009.

Patients with evidence of joint inflammation should start a combination of disease-modifying drugs (DMARD) as soon as possible. Other important treatment options include analgesia, physiotherapy and surgery.

Initial therapy

- in the 2009 NICE guidelines it is recommend that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids)

DMARDs

- methotrexate is the most widely used DMARD. Monitoring of FBC & LFTs is essential due to the risk of myelosuppression and liver cirrhosis. Other important side-effects include pneumonitis
- sulfasalazine
- leflunomide
- hydroxychloroquine

TNF-inhibitors

- the current indication for a TNF-inhibitor is an inadequate response to at least two DMARDs including methotrexate
- etanercept: recombinant human protein, acts as a decoy receptor for TNF- α , subcutaneous administration, can cause demyelination, risks include reactivation of tuberculosis
- infliximab: monoclonal antibody, binds to TNF- α and prevents it from binding with TNF receptors, intravenous administration, risks include reactivation of tuberculosis
- adalimumab: monoclonal antibody, subcutaneous administration

Rituximab

- anti-CD20 monoclonal antibody, results in B-cell depletion
- two 1g intravenous infusions are given two weeks apart
- infusion reactions are common

Abatacept

- fusion protein that modulates a key signal required for activation of T lymphocytes
- leads to decreased T-cell proliferation and cytokine production
- given as an infusion
- not currently recommend by NICE

Enter your notes here...

Save my notes

A 40-year-old woman who is known to have systemic lupus erythematosus is reviewed with an exacerbation of wrist pain. Which one of the following is the most useful marker for monitoring disease activity?

☐	C-reactive protein
☐	C2 levels
☐	Anti-nuclear antibody titres
☐	Anti-dsDNA titres
☐	Anti-Sm titres

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☐	Anti-Sm titres

Submit answer

SLE: investigations

Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)
- also: anti-U1 RNP, SS-A (anti-Ro) and SS-B (anti-La)

Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2636062/>

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Save my notes

Which one of the following is not associated with carpal tunnel syndrome?

- | | |
|-----------------------|--|
| ☐ | Tinel's sign |
| ☐ | Compression of the median nerve |
| ☐ | Wasting of the hypothenar eminence |
| ☐ | Flexion of the wrist reproduces symptoms |
| ☐ | Weakness of thumb abduction |

Submit answer

د. عاصم وراز ©

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Submit answer

د. عاصم وراز ©

Carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of median nerve in the carpal tunnel.

History

- pain/pins and needles in thumb, index, middle finger
- unusually the symptoms may 'ascend' proximally
- patient shakes his hand to obtain relief, classically at night

Examination

- weakness of thumb abduction (abductor pollicis brevis)
- wasting of thenar eminence (NOT hypothenar)
- Tinel's sign: tapping causes paraesthesia
- Phalen's sign: flexion of wrist causes symptoms

Causes

- idiopathic
- pregnancy
- oedema e.g. heart failure
- lunate fracture
- rheumatoid arthritis

Electrophysiology

- motor + sensory: prolongation of the action potential

Treatment

- corticosteroid injection
- wrist splints at night
- surgical decompression (flexor retinaculum division)

A 34-year-old kitchen worker presents with a two week history of pain in her right wrist. She has recently emigrated from Ghana and has no past medical history of note. On examination she is tender over the base of her right thumb and also over the radial styloid process. Ulnar deviation of the wrist recreates the pain. What is the most likely diagnosis?

☐	Rheumatoid arthritis
☐	Osteoarthritis of the carpometacarpal joint
☐	De Quervain's tenosynovitis
☐	Carpal tunnel syndrome
☐	Systemic lupus erythematosus

Submit answer

د. عاصم وراز ©

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د. عاصم وراز ©

De Quervain's tenosynovitis

De Quervain's tenosynovitis is a common condition in which the sheath containing the extensor pollicis brevis and abductor pollicis longus tendons is inflamed. It typically affects females aged 30 - 50 years old

Features

- pain on the radial side of the wrist
- tenderness over the radial styloid process
- abduction of the thumb against resistance is painful
- Finkelstein's test: with the thumb is flexed across the palm of the hand, pain is reproduced by movement of the wrist into flexion and ulnar deviation

Management

- analgesia
- steroid injection
- immobilisation with a thumb splint (spica) may be effective
- surgical treatment is sometimes required

A 54-year-old man is diagnosed as having gout. You are discussing ways to help prevent future attacks. Which one of the following is most likely to precipitate an attack of gout?

☐	Chocolate
☐	Brazil nuts
☐	Eggs
☐	Sardines
☐	Smoking

Submit answer

د. جاسم وراز ©

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Submit answer

د. جاسم وراز ©

Foods to avoid include those high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid $> 450 \mu\text{mol/l}$)

Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine* has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of $< 300 \mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol**

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

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A 45-year-old man presents with a painful, swollen and red left middle toe. There is no history of trauma and his symptoms have been present for around a week. Which one of the following conditions is most associated with this presentation?

☐	Diabetes mellitus
☐	Systemic sclerosis
☒	Rheumatoid arthritis
☐	Bisphosphonate use
☐	Psoriatic arthritis

Submit answer

د. عاصم ویرانز ©

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د. عاصم دراز ©

A 'sausage-shaped' digit is a classical description of dactylitis. It would be unusual for gout to affect the middle toe, the vast majority of cases occur in the first metatarsophalangeal joint.

The lack of systemic upset, length of history and confined erythema go against a diagnosis of septic arthritis (e.g. linked to diabetes).

Dactylitis is not a feature of rheumatoid arthritis.

Dactylitis

Dactylitis describes the inflammation of a digit (finger or toe).

Causes include:

- spondyloarthritis: e.g. Psoriatic and reactive arthritis
- sickle-cell disease
- other rare causes include tuberculosis, sarcoidosis and syphilis

A 27-year-old woman is referred to orthopaedics. Three years she had surgery and chemotherapy for thyroid cancer. Follow up scans to date have shown no evidence of any disease recurrence. For the past two months she has been experiencing gradually increasing pain in her right hip which is worse on exercising. On examination passive movement of the hip is painful in all directions, especially internal rotation. An x-ray ordered by her GP has been reported as normal. What is the most likely diagnosis?

☐	Trochanteric bursitis
☐	Avascular necrosis of the femoral head
☐	Primary hyperparathyroidism
☐	Metastatic deposits
☐	Hypoparathyroidism

Submit answer

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Submit answer

د. حاصم وراز ©

Initial x-rays are often normal in patients with avascular necrosis, but it would be unlikely that metastatic deposits significant enough to cause pain would not be shown.

Avascular necrosis

Avascular necrosis (AVN) may be defined as death of bone tissue secondary to loss of the blood supply. This leads to bone destruction and loss of joint function. It most commonly affects the epiphysis of long bones such as the femur.

Causes

- long-term steroid use
- chemotherapy
- alcohol excess
- trauma

Features

- initially asymptomatic
- pain in the affected joint

Investigation

- plain x-ray findings may be normal initially
- MRI is the investigation of choice. It is more sensitive than radionuclide bone scanning

A 73-year-old man presents pain in his right thigh. This has been getting progressively worse for the past 9 months despite being otherwise well. An x-ray is reported as follows:

X-ray right femur	Radiolucency of subarticular region suggestive of osteolysis. Some areas of patchy sclerosis
-------------------	--

Bloods tests show:

Calcium	2.38 mmol/l
Phosphate	0.85 mmol/l
Alkaline phosphatase	544 u/L
Prostate specific antigen	4.4 ng/ml

What is the most appropriate action?

☐	Vitamin D supplementation
☐	Check serum testosterone
☐	Referral to an orthopaedic surgeon
☐	Referral to a urologist
☐	IV bisphosphonates

Submit answer

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Submit answer

This patient has Paget's disease as evidenced by an isolated rise in ALP and characteristic x-ray changes. As he has bone pain he should be treated with bisphosphonates. A PSA of 4.4 ng/ml is probably normal in a 73-year-old man and is certainly not consistent with metastatic prostate cancer.

Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

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A 25-year-old man presents with a painful, swollen left knee. He returned 4 weeks ago from a holiday in Spain. There is no history of trauma and he has had no knee problems previously. On examination he has a swollen, warm left knee with a full range of movement. His ankle joints are also painful to move but there is no swelling. On the soles of both feet you notice a waxy yellow rash. What is the most likely diagnosis?

☐	Rheumatoid arthritis
☐	Psoriatic arthritis
☐	Gout
☐	Reactive arthritis
☐	Gonococcal arthritis

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Submit answer

د. جاسم وراز ©

The rash on the soles is keratoderma blenorrhagica. His reactive arthritis may be secondary to either gastrointestinal infection or *Chlamydia*.

Reactive arthritis: features

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

Features

- typically develops within 4 weeks of initial infection - symptoms generally last around 4-6 months
- arthritis is typically an asymmetrical oligoarthritis of lower limbs
- dactylitis
- symptoms of urethritis
- eye: conjunctivitis (seen in 50%), anterior uveitis
- skin: circinate balanitis (painless vesicles on the coronal margin of the prepuce), keratoderma blenorrhagica (waxy yellow/brown papules on palms and soles)

Around 25% of patients have recurrent episodes whilst 10% of patients develop chronic disease



Keratoderma blenorrhagica

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Next question

A 24-year-old man is investigated for chronic back pain. Which one of the following would most suggest a diagnosis of ankylosing spondylitis?

☐	Reduced lateral flexion of the lumbar spine
☐	Pain gets worse during the day
☐	Accentuated lumbar lordosis
☐	Pain on straight leg raising
☐	Loss of thoracic kyphosis

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د. عاصم دراز ©

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Submit answer

د. عاصم دراز ©

Reduced lateral flexion of the lumbar spine is one of the earliest signs of ankylosing spondylitis. There tends to be a loss of lumbar lordosis and an accentuated thoracic kyphosis in patients with ankylosing spondylitis

Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

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A 45-year-old man who is known to have haemochromatosis presents with a swollen and painful right knee. An x-ray shows no fracture but extensive chondrocalcinosis. Given the likely diagnosis, which one of the following is most likely to present in the joint fluid?

- | | |
|-----------------------|--|
| ☐ | Raised hyaluronic acid levels |
| ☐ | Monosodium urate crystals |
| ☐ | Bipyramidal oxalate crystals |
| ☐ | Negatively birefringent calcium carbonate crystals |
| ☐ | Positively birefringent rhomboid-shaped crystals |

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د. حاصم وراز ©

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Submit answer

د. حاصم وراز ©

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

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Which of the following statements is true regarding psoriatic arthropathy?

☐	Skin disease always precedes joint disease
☐	Approximately one-third of patients with psoriasis eventually develop arthropathy
☐	The mainstay of management is analgesia, physiotherapy and joint replacement
☐	Males and females are equally affected
☐	Arthritis mutilans is the most common subtype

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Males and females are affected equally by psoriatic arthritis

Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10% percent of patients with skin lesions develop an arthropathy with males and females being equally affected

Types*

- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management

- treat as rheumatoid arthritis
- but better prognosis

*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies

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Which one of the following is most recognised as a risk factor for developing osteoporosis?

- | | |
|-----------------------|-----------------------------|
| ☐ | Osteogenesis imperfecta |
| ☐ | Marfan's syndrome |
| ☐ | Myotonic dystrophy |
| ☐ | Duchenne muscular dystrophy |
| ☐ | Ehler-Danlos syndrome |

Submit answer

د. عاصم دراز ©

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Marfan's syndrome



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Duchenne muscular dystrophy



Ehler-Danlos syndrome

Submit answer

د. عاصم وراز ©

Osteoporosis: causes

Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

*research is ongoing as to whether warfarin is a risk factor

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A 71-year-old man presents with an erythematous, swollen first metatarsophalangeal joint on the left foot. This is causing him considerable pain and he is having difficulty walking. He has never had any previous similar episodes. His past medical history includes atrial fibrillation and type 2 diabetes mellitus and his current medications are warfarin, metformin and simvastatin. What is the most appropriate treatment of this episode?

☐	Intra-articular corticosteroid
☐	Colchicine
☐	Ibuprofen
☐	Diclofenac
☐	Prednisolone

Submit answer

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Submit answer

NSAIDs should be avoided in elderly patients taking warfarin due to the risk of a life-threatening gastrointestinal haemorrhage. Oral steroids are an option but would upset his diabetic control.

Whilst anticoagulation is not a contraindication to joint injection it would make this option less attractive

Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450 $\mu\text{mol/l}$)

Acute management

- NSAIDs
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Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
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Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
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*inhibits microtubule polymerization by binding to tubulin, interfering with mitosis. Also inhibits neutrophil motility and activity

**patients with Lesch-Nyhan syndrome often take allopurinol for life

Enter your notes here...

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A 33-year-old female presents 6 weeks after the birth of her first child with a two-week history of polyarthralgia, fever and a skin rash. First-line investigations show:

ESR	45 mm/hour
-----	------------

What is the most likely diagnosis?

- | | |
|-----------------------|-----------------------------------|
| ☐ | Polymorphic eruption of pregnancy |
| ☐ | Systemic lupus erythematosus |
| ☐ | Rheumatoid arthritis |
| ☐ | Reactive arthritis |
| ☐ | Pseudogout |

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د. عاصم دراز ©

Unlike many autoimmune diseases systemic lupus erythematosus (SLE) often becomes worse during pregnancy and the puerperium

SLE: pregnancy

Overview

- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematosus
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies

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Save my notes

A 57-year-old woman with a history of polymyalgia rheumatica has been taking prednisolone 10 mg for the past 5 months. A DEXA scan is reported as follows:

L2 T-score	-1.6 SD
Femoral neck T-score	-1.7 SD

What is the most suitable management?

☐	No treatment
☐	Vitamin D + calcium supplementation + repeat DEXA scan in 6 months
☐	Vitamin D + calcium supplementation
☐	Vitamin D + calcium supplementation + hormone replacement therapy
☐	Vitamin D + calcium supplementation + oral bisphosphonate

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Submit answer

This patient has been taking 10mg of prednisolone for the past 5 months and hence should be assessed for bone protection. The T score of less than -1.5 SD is an indication for a bisphosphonate. This should be co-prescribed with calcium + vitamin D.

Osteoporosis: glucocorticoid-induced

Patients who take the equivalent of prednisolone 7.5 mg or more each day for 3 months or longer should be assessed and where necessary given prophylactic treatment

Assessment for treatment - patients taking the equivalent of prednisolone 7.5 mg or more each day for 3 months, and one of the following

- are over the age of 65 years
- have a history of a fragility fracture
- have a T-score less than - 1.5 SD

Treatment

- first-line: oral bisphosphonate
- second-line: alfacalcidol or calcitriol

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Osteoporosis: glucocorticoid-induced new

We know that one of the most important risk factors for osteoporosis is the use of corticosteroids. As these drugs are so widely used in clinical practice it is important we manage this risk appropriately.

The most widely followed guidelines are based around the 2002 Royal College of Physicians (RCP) 'Glucocorticoid-induced osteoporosis: A concise guide to prevention and treatment'.

The risk of osteoporosis is thought to rise significantly once a patient is taking the equivalent of prednisolone 7.5mg a day for 3 or more months. It is important to note that we should manage patients in an anticipatory, i.e. if it likely that the patient will have to take steroids for at least 3 months then we should start bone protection straight away, rather than waiting until 3 months has elapsed. A good example is a patient with newly diagnosed polymyalgia rheumatica. As it is very likely they will be on a significant dose of prednisolone for greater than 3 months bone protection should be commenced immediately.

Management of patients at risk of corticosteroid-induced osteoporosis

The RCP guidelines essentially divide patients into two groups.

- 1. Patients over the age of 65 years or those who've previously had a fragility fracture should be offered bone protection.
- 2. Patients under the age of 65 years should be offered a bone density scan, with further management dependent:

T score	Management
Greater than 0	Reassure
Between 0 and -1.5	Repeat bone density scan in 1-3 years
Less than -1.5	Offer bone protection

The first-line treatment is alendronate. Patients should also be calcium and vitamin D replete.

Which one of the following would not suggest an underlying connective tissue disorder in a patient with Raynaud's?

☐	Unilateral symptoms
☐	Digital ulcers
☐	Presence of autoantibodies
☐	Onset at 25 years old
☐	Calcinosis

Submit answer

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Submit answer

Raynaud's disease (i.e. primary) presents in young women with bilateral symptoms

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

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A 66-year-old female presents with pain at the base of her left thumb. She has no past medical history of note. On examination there is diffuse tenderness and swelling of her left first carpometacarpal joint. What is the most likely diagnosis?

☐	Osteoarthritis
☐	De Quervain's tenosynovitis
☐	Gout
☐	Rheumatoid arthritis
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Submit answer

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Submit answer

د. عامر وراز ©

The trapeziometacarpal joint (base of thumb) is the most common site of hand osteoarthritis.

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

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A 66-year-old female is on long-term prednisolone therapy for polymyalgia rheumatica. What is the most appropriate protection against osteoporosis?

☐	Hormone replacement therapy
☐	Calcitonin
☐	Oral bisphosphonate
☐	Calcium and vitamin D
☐	Hip-protectors

Submit answer

د. عاصم وراز ©

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Submit answer

د. عامر وراز ©

Oral bisphosphonate therapy is recommended for patients older than 65 years who have taken, or who are likely to remain on oral corticosteroids for more than 3 months

Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

A 54-year-old woman is reviewed. She was discharged from the psychiatric ward around 5 weeks ago following an admission for an acute psychotic episode. Her psychotic symptoms have settled on risperidone but unfortunately she has now developed a dry mouth and arthralgia in both hands. A number of blood tests are requested:

Rheumatoid factor	Positive
Anti-Ro	Positive
Anti-Smith	Negative
ANA	Positive
C4	Low

What is the most likely diagnosis?

☐	Systemic lupus erythematosus
☐	Sarcoidosis
☐	Drug-induced lupus erythematosus
☐	Rheumatoid arthritis
☐	Sjogren's syndrome

Submit answer

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Submit answer

Risperidone (unlike chlorpromazine) is not a common trigger of lupus. Anti-Ro is positive in around 70% of patients with Sjogren's syndrome compared to around 10% of patients with rheumatoid arthritis

Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

Management

- artificial saliva and tears
- pilocarpine may stimulate saliva production

Enter your notes here...



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Which one of the following is most likely to indicate an underlying connective tissue disorder in a patient with Raynaud's phenomenon?

☐	Chilblains
☐	Bilateral symptoms
☐	Female patient
☐	Onset at 18 years old
☐	Recurrent miscarriages

Submit answer

د. حاصیہ وراز ©

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☒	Recurrent miscarriages

Submit answer

د. حاصیہ وراز ©

Raynaud's disease (i.e. primary) presents in young women with bilateral symptoms

A history of recurrent miscarriages could indicate systemic lupus erythematosus or anti-phospholipid syndrome. Chilblains (pernio) are itchy, painful purple swellings which occur on the fingers and toes after exposure to the cold. They are occasionally associated with underlying connective tissue disease but this is rare

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

Enter your notes here...



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A 33-year-old female is admitted to the Emergency Department due to right-sided weakness. She has a past history of deep vein thrombosis following the birth of her daughter. The only other past history of note is two miscarriages. A CT head confirms an ischaemic stroke in the left middle cerebral artery territory. What is the likely finding on echocardiography?

☐	Normal
☐	Dilated cardiomyopathy
☐	Bicuspid aortic valve
☐	Atrial septal defect
☐	Ventricular septal defect

Submit answer

د. جاسم وراز ©

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د. حاصو وراز ©

This is a typical MRCP question. On first sight this question appears to be pointing towards a paradoxical embolus. However, given the history of miscarriages and DVT a diagnosis of antiphospholipid syndrome is more likely.

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

A 35-year-old woman who has severe Raynaud's disease is reviewed in clinic. Three months ago she was started on nifedipine. Unfortunately this has had a minimal effect on her symptoms and has resulted in ankle oedema. What is the most appropriate next step in management?

☐	Aspirin
☐	Sympathectomy
☐	Intravenous prostacyclin
☐	Methotrexate
☐	Intravenous infliximab

Submit answer

د. عاصم وراز ©

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Enter your notes here...

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A 63-year-old man presents to the Emergency Department with a 2 day history of a painful and swollen left knee joint. Aspiration reveals positively birefringent crystals and no organisms are seen. Which of the following conditions are not recognised causes of the underlying condition?

- | | |
|-----------------------|---------------------|
| ☐ | Haemochromatosis |
| ☐ | Low magnesium |
| ☐ | High phosphate |
| ☐ | Acromegaly |
| ☐ | Hyperparathyroidism |

Submit answer

د. عاصم وراز ©

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Low magnesium



High phosphate



Acromegaly



Hyperparathyroidism

Submit answer

د. عامر وراز ©

A low phosphate predisposes to pseudogout

Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

Enter your notes here...

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A 23-year-old female presents with a painful ankle following an inversion injury whilst playing tennis. Which one of the following findings is least relevant when deciding whether an x-ray is needed?

☐	Swelling immediately after the injury and now
☐	Pain in the malleolar zone
☐	Tenderness at the medial malleolar zone
☐	Tenderness at the lateral malleolar zone
☐	Cannot walk 4 steps immediately after the injury and now

Submit answer

د. عاصم وراز ©

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Submit answer

د. عاصم وراز ©

Ankle injury: Ottawa rules

The Ottawa Rules with for ankle x-rays have a sensitivity approaching 100%

An ankle x-ray is required only if there is any pain in the malleolar zone and any one of the following findings:

- bony tenderness at the lateral malleolar zone (from the tip of the lateral malleolus to include the lower 6 cm of posterior border of the fibular)
- bony tenderness at the medial malleolar zone (from the tip of the medial malleolus to the lower 6 cm of the posterior border of the tibia)
- inability to walk four weight bearing steps immediately after the injury and in the emergency department

There are also Ottawa rules available for both foot and knee injuries

Enter your notes here....

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A 28-year-old man is diagnosed with having ankylosing spondylitis. He presented with a six month history of back pain. On examination there is reduced lateral flexion of the spine but no evidence of any other complications. Which one of the following is he most likely to offered as first-line treatment?

☐	Exercise regime + NSAIDs
☐	Exercise regime + infliximab
☐	Physiotherapy + sulfasalazine
☐	Physiotherapy + etanercept
☐	Exercise regime + paracetamol

Submit answer

د. حاصی وراز ©

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Submit answer

د. حاصو وراز ©

The anti-TNF drugs are currently only used for patients with severe ankylosing spondylitis which has failed to respond to NSAIDs.

Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 3:1) aged 20-30 years old.

Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis.

Radiographs may be normal early in disease, later changes include:

- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- syndesmophytes: due to ossification of outer fibers of annulus fibrosus
- chest x-ray: apical fibrosis



© Image used on license from Radiopaedia

40-year-old male. There is typical appearance of bamboo spine with a single central radiodense line related to ossification of supraspinous and interspinous ligaments which is called dagger sign. Ankylosing is detectable in both sacroiliac joints



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Ankylosing spondylitis with well formed syndesmophytes



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Lateral cervical spine. Complete fusion of anterior and posterior elements in ankylosing spondylitis, so called bamboo spine



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Fusion of bilateral sacroiliac joints. Sacroilitis may present as sclerosis of joint margins which can be asymmetrical at early stage of disease, but is bilateral and symmetrical in late disease



© Image used on license from Radiopaedia

Syndesmophytes and squaring of vertebral bodies. Squaring of anterior vertebral margins is due to osteitis of anterior corners. Syndesmophytes are due to ossification of outer fibers of annulus fibrosus

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

Management

The following is partly based on the 2010 EULAR guidelines (please see the link for more details):

- encourage regular exercise such as swimming
- physiotherapy
- NSAIDs are the first-line treatment
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- the 2010 EULAR guidelines suggest: 'Anti-TNF therapy should be given to patients with persistently high disease activity despite conventional treatments'
- research is ongoing to see whether anti-TNF therapies such as etanercept and adalimumab should be used earlier in the course of the disease

د. حاصو وراثر ©

Which one of the following is most consistently associated with a poor prognosis in rheumatoid arthritis?

☐	Anti-CCP antibodies
☐	HLA DR2 allele
☐	Rapid onset
☐	Being a smoker
☐	Female sex

Submit answer

د. حاصیہ وراز ©

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د. حاصی وراز ©

See below for further information on the effect of gender on prognosis.

Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

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You review a 40-year-old mechanic who presents with joint pains. For the past two months he has noticed intermittent pain, stiffness and swelling of the joints in his hands and feet. The stiffness tends to improve during the day but the pain tends to get worse. He has also noticed stiffness in his back but cannot remember any aggravating injury. You order some blood tests (taken during an acute attack) which are reported as follows:

Rheumatoid factor	Negative
Anti-cyclic citrullinated peptide antibody	Positive
Uric acid	0.3 mmol/l (0.18 - 0.48)
ESR	41 mm/hr

What is the most likely diagnosis?

☐	Reactive arthritis
☐	Ankylosing spondylitis
☐	Gout
☐	Osteoarthritis
☐	Rheumatoid arthritis

Submit answer

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☐	Osteoarthritis
☒	Rheumatoid arthritis

Submit answer

Anti-cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis

Anti-cyclic citrullinated peptide antibody is highly specific for rheumatoid arthritis.

Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

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A 30-year-old female who is known to have antiphospholipid syndrome is diagnosed as having a deep vein thrombosis. This is her first thrombotic event. How should her anticoagulation be managed?

- | | |
|-----------------------|--|
| ☐ | Life-long low-dose aspirin |
| ☐ | 6 months warfarin, target INR 2 - 3 |
| ☐ | Life-long warfarin, target INR 3 - 4 |
| ☐ | Life-long warfarin, target INR 2 - 3 |
| ☐ | 6 months warfarin, target INR 2 - 3 followed by life-long low-dose aspirin and clopidogrel |

Submit answer

د. عاصم دراز ©

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Submit answer

د. عاصم دراز ©

This is a tough question and some textbooks may contradict this answer, suggesting either lifelong warfarin or a target INR of 3-4. Please see the link to the BCSH guidelines. There is also a recent review in JAMA 2006; 295(9): 1050-7

Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

A 20-year-old woman is reviewed in the rheumatology clinic. She has been referred due to a three month history of arthralgia, lethargy, muscle pains and Raynaud's phenomenon. On examination she is noted to have slightly swollen hands but no significant synovitis. A number of blood tests are ordered:

Hb	12.9 g/dl
Platelets	$282 \times 10^9/l$
WBC	$6.2 \times 10^9/l$

Rheumatoid factor	Negative
ANA	Positive
Anti-dsDNA antibodies	Negative
CRP	25 mg/l
ESR	39 mm/hr
Creatine kinase	675 ng/mL (50-200)

Given the likely diagnosis, which other antibodies are most likely to be present?

☐	Anti-Scl-70
☐	Anti-centromere
☐	Anti-Jo
☐	Anti-RO
☐	Anti-RNP

Submit answer

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☐	Anti-Jo
☐	Anti-RO
☒	Anti-RNP

Submit answer

Anti-ribonuclear protein (anti-RNP) = mixed connective tissue disease

This patient has typical features of mixed connective tissue disease (e.g. arthralgia, myositis and Raynaud's). To confirm the diagnosis anti-RNP antibodies need to be detected.

Mixed connective tissue disease

Features of SLE, systemic sclerosis and polymyositis

Anti-RNP positive

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A 62-year-old man with lung cancer is suspected of having dermatomyositis. Which one of the following antibodies is most likely to be positive?

☐	Anti-nuclear antibodies
☐	Anti-centromere bodies
☐	Anti-scl-70 antibodies
☐	Anti-Jo-1 antibodies
☐	Anti-Mi-2 antibodies

Submit answer

د. حاصیہ وراز ©

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☐	Anti-Mi-2 antibodies

Submit answer

د. حاصی وراز ©

Dermatomyositis antibodies: ANA most common, anti-Mi-2 most specific

Dermatomyositis: investigations and management

Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever

Management

- prednisolone

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A 50-year-old woman complains of pain in her right elbow. This has been present for the past four weeks and is maximal around 4-5cm distal from the lateral aspect of the elbow joint. The pain is made worse by extending the elbow and pronating the forearm. What is the most likely diagnosis?

☐	Lateral epicondylitis
☐	Radial tunnel syndrome
☐	De Quervain's tenosynovitis
☐	Cubital tunnel syndrome
☐	Medial epicondylitis

Submit answer

د. عاصم وراز ©

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د. عاصم وراز ©

Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

Lateral epicondylitis (tennis elbow)	Features • pain and tenderness localised to the lateral epicondyle • pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended • episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks
Medial epicondylitis (golfer's elbow)	Features • pain and tenderness localised to the medial epicondyle • pain is aggravated by wrist flexion and pronation • symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement
Radial tunnel syndrome	Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse. Features • symptoms are similar to lateral epicondylitis making it difficult to diagnose • however, the pain tends to be around 4-5 cm distal to the lateral epicondyle • symptoms may be worsened by extending the elbow and pronating the forearm
Cubital tunnel syndrome	Due to the compression of the ulnar nerve. Features • initially intermittent tingling in the 4th and 5th finger • may be worse when the elbow is resting on a firm surface or flexed for extended periods • later numbness in the 4th and 5th finger with associated weakness
Olecranon bursitis	Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.

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Which one of the following antibodies is most specific for systemic lupus erythematosus?

☐	Anti-neutrophil cytoplasmic antibodies
☐	Anti-nuclear antibodies
☐	Anti-Sm antibodies
☐	Anti-RNP antibodies
☐	Anti-cardiolipin antibodies

Submit answer

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Submit answer

SLE: ANA is 99% sensitive - anti-Sm & anti-dsDNA are 99% specific

SLE: investigations

Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)
- also: anti-U1 RNP, SS-A (anti-Ro) and SS-B (anti-La)

Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Enter your notes here....

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Which one of the following is most recognised as a potential complication in a patient with ankylosing spondylitis?

☐	Heart block
☐	Aortic stenosis
☐	Achalasia
☐	Diabetes mellitus
☐	Bronchiectasis

Submit answer

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Submit answer

Ankylosing spondylitis features - the 'A's'

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis

Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

Other features - the 'A's'

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

A 58-year-old woman with a history of left hip osteoarthritis presents for review. She is currently taking co-codamol 30/500 for pain on a regular basis but this is unfortunately not controlling her symptoms. There is no past medical history of note, in particular no asthma or gastrointestinal problems. What is the most suitable next step in management?

☐	Switch to regular oral tramadol
☐	Add topical ibuprofen
☐	Add oral diclofenac + proton pump inhibitor
☐	Add oral etoricoxib
☐	Add oral diclofenac

Submit answer

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Submit answer

Topical NSAIDs are only indicated for osteoarthritis of the knee or hand.

Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Which one of the following is least associated with the development of gout?

☐	Psoriasis
☒	Lesch-Nyhan syndrome
☐	Lymphoma
☐	Lithium toxicity
☐	Renal failure

Submit answer

د. حاصیہ وراز ©

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Submit answer

د. حاصیہ وراز ©

Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid

- drugs*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid

- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome

- hypoxanthine-guanine phosphoribosyl transferase (HGPRTase) deficiency
- x-linked recessive
- features: gout, renal failure, neurological deficits, learning difficulties, self-mutilation

*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

A 44-year-old woman is seen in the rheumatology clinic. She has been referred with Raynaud's phenomenon. During the review of systems she mentions that her GP is organising an endoscopy to investigate dyspepsia. On examination she is noted to have tight, shiny skin over her fingers. Which one of the following complications is she most likely to develop?

☐	Bronchiectasis
☐	Angiodysplasia
☐	Arterial hypertension
☐	Chronic kidney disease
☐	Pulmonary hypertension

Submit answer

د. عاصم وراز ©

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د. عاصم وراز ©

This patient is likely to have CREST syndrome. Unfortunately pulmonary hypertension is one of the more common late complications seen in such patients.

Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear



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Antibodies

- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

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Save my notes

A 41-year-old female presents with lethargy and pain all over her body. This has been present for the past six months and is often worse when she is stressed or cold. Clinical examination is unremarkable other than a large number of tender points throughout her body. A series of blood tests including an autoimmune screen, inflammatory markers and thyroid function are normal. Given the likely diagnosis, which one of the following is not helpful in management?

☐	Amitriptyline
☐	Trigger point injections
☐	Cognitive behavioural therapy
☐	Exercise programme
☐	Paracetamol

Submit answer

د. عاصم وراز ©

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Submit answer

د. عاصم وراز ©

A recent JAMA paper supported the use of anti-depressants in fibromyalgia

Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis; 2009 Jan 14;301(2):198-209

Fibromyalgia

Fibromyalgia is a syndrome characterised by widespread pain throughout the body with tender points at specific anatomical sites. The cause of fibromyalgia is unknown.

Epidemiology

- women are 10 times more likely to be affected
- typically presents between 30-50 years old

Features

- pain: at multiple site, sometimes 'pain all over'
- lethargy
- sleep disturbance, headaches, dizziness are common

Diagnosis is clinical and sometimes refers to the American College of Rheumatology classification criteria which lists 9 pairs of tender points on the body. If a patient is tender in at least 11 of these 18 points it makes a diagnosis of fibromyalgia more likely

The management of fibromyalgia is often difficult and needs to be tailored to the individual patient. A psychosocial and multidisciplinary approach is helpful. Unfortunately there is currently a paucity of evidence and guidelines to guide practice. The following is partly based on consensus guidelines from the European League against Rheumatism (EULAR) published in 2007.

- explanation
- exercise programme
- cognitive behavioural therapy
- anti-depressants: amitriptyline

Enter your notes here...



Save my notes

د. حاصو وراز ©

A 47-year-old female is referred to the rheumatology clinic due to cold fingers. Which connective tissue disease is most strongly associated with Raynaud's phenomenon?

☐	Systemic lupus erythematosus
☐	Rheumatoid arthritis
☐	Systemic sclerosis
☐	Sjogren's syndrome
☐	Polyarteritis nodosa

Submit answer

د. عاصم وراز ©

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Submit answer

د. ناصر وراز ©

Raynaud's phenomenon is associated with all the above conditions but is most strongly linked to systemic sclerosis. Around 2% of women and 6% of men with Raynaud's phenomenon develop systemic sclerosis

Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

Enter your notes here...

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Which one of the following is the most common ocular manifestation of rheumatoid arthritis?

☐	Scleritis
☐	Episcleritis
☐	Keratoconjunctivitis sicca
☐	Corneal ulceration
☐	Keratitis

Submit answer

د. عاصم وراز ©

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Submit answer

د. عاصم وراز ©

Keratoconjunctivitis sicca is characterised by dry, burning and gritty eyes caused by decreased tear production

Rheumatoid arthritis: ocular manifestations

Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

Ocular manifestations

- keratoconjunctivitis sicca (most common)
- episcleritis (erythema)
- scleritis (erythema and pain)
- corneal ulceration
- keratitis

Iatrogenic

- steroid-induced cataracts
- chloroquine retinopathy

Which one of the following drugs is least likely to cause gout?

☐	Lithium
☐	Bendrofluazide
☐	Alcohol
☐	Pyrazinamide
☐	Furosemide

Submit answer

د. عاصم دراز ©

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☐	Furosemide

Submit answer

د. عاصم دراز ©

Lithium was actually used to treat gout in the 19th century

Gout: drug causes

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Drug causes

- thiazides, furosemide
- alcohol
- cytotoxic agents
- pyrazinamide

A 39-year-old woman with a history of rheumatoid arthritis presents with a two day history of a red right eye. There is no itch or pain. Pupils are 3mm, equal and reactive to light. Visual acuity is 6/5 in both eyes. What is the most likely diagnosis?

☐	Keratoconjunctivitis sicca
☐	Scleritis
☐	Glaucoma
☐	Episcleritis
☐	Anterior uveitis

Submit answer

د. حاصو وراز ©

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د. حاصو وراز ©

Scleritis is painful, episcleritis is not painful

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Which one of the following is most useful in the management of Familial Mediterranean Fever?

☐	Prednisolone
☐	Erythromycin
☐	Cyclophosphamide
☐	Colchicine
☐	Benzylopenicillin

Submit answer

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☐	Benzympenicillin

Submit answer

Familial Mediterranean Fever

Familial Mediterranean Fever (FMF, also known as recurrent polyserositis) is an autosomal recessive disorder which typically presents by the second decade. It is more common in people of Turkish, Armenian and Arabic descent

Features - attacks typically last 1-3 days

- pyrexia
- abdominal pain (due to peritonitis)
- pleurisy
- pericarditis
- arthritis
- erysipeloid rash on lower limbs

Management

- colchicine may help

A 64-year-old female is referred to rheumatology out-patients by her GP with a history of arthritis in both hands. Which one of the following x-ray findings would most favour a diagnosis of rheumatoid arthritis over other possible causes?

☐	Loss of joint space
☐	Periarticular osteopenia
☐	Subchondral sclerosis
☐	Osteophytes
☐	Subchondral cysts

Submit answer

د. عاصم وراز ©

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Submit answer

د. حاصو وراز ©

Periarticular osteopenia and osteoporosis would point towards a diagnosis of rheumatoid arthritis (RA).
Loss of joint space is common in both RA and osteoarthritis

Rheumatoid arthritis: x-ray changes

Early x-ray findings

- loss of joint space
- juxta-articular osteoporosis
- soft-tissue swelling

Late x-ray findings

- periarticular erosions
- subluxation

A 33-year-old man who is suspected of having ankylosing spondylitis has a lumbar spine x-ray. Which one of the following features is most likely to be present?

☐	Wedge shaped discs
☐	Sclerosis
☐	'Rugger-Jersey' spine
☐	Osteophytes
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Submit answer

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Submit answer

د. جاسم وراز ©

Ankylosing spondylitis - x-ray findings: subchondral erosions, sclerosis and squaring of lumbar vertebrae

Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

Enter your notes here...



Save my notes

A 31-year-old woman who had rheumatoid arthritis diagnosed 5 years ago asks for advice as she is considering starting a family. She currently has quiescent rheumatoid arthritis which is well controlled on methotrexate. Which one of the following drugs is it safest to use if she is planning on becoming pregnant?

☐	Leflunamide
☐	Sulfasalazine
☐	Methotraxate
☐	Rituximab
☐	Gold

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☐	Gold

Rheumatoid arthritis: pregnancy

Rheumatoid arthritis (RA) typically develops in women of a reproductive age. Issues surrounding conception are therefore commonly encountered. There are no current published guidelines regarding how patients considering conception should be managed although expert reviews are largely in agreement.

Key points

- patients with early or poorly controlled RA should be advised to defer conception until their disease is more stable
- RA symptoms tend to improve in pregnancy but only resolve in a small minority. Patients tend to have a flare following delivery
- methotrexate is not safe in pregnancy and needs to be stopped at least 3 months before conception
- leflunomide is not safe in pregnancy
- sulfasalazine and hydroxychloroquine are considered safe in pregnancy
- interestingly studies looking at pregnancy outcomes in patients treated with TNF- α blockers do not show any significant increase in adverse outcomes. It should be noted however that many of the patients included in the study stopped taking TNF- α blockers when they found out they were pregnant
- low-dose corticosteroids may be used in pregnancy to control symptoms
- NSAIDs may be used until 32 weeks but after this time should be withdrawn due to the risk of early close of the ductus arteriosus
- patients should be referred to an obstetric anaesthetist due to the risk of atlanto-axial subluxation

Answer B

A 57-year-old woman presents with a three month history of right-sided hip pain. This seems to have come on spontaneously without any obvious precipitating event. The pain is described as being worse on the 'outside' of the hip and is particularly bad at night when she lies on the right hand side.

On examination there is a full range of movement in the hip including internal and external rotation. Deep palpation of the lateral aspect of the right hip joint recreates the pain.

An x-ray of the right hip is reported as follows:

Right hip: Minor narrowing of the joint space otherwise normal appearance

What is the most likely diagnosis?

☐	Fibromyalgia
☐	Lumbar nerve root compression
☐	Osteoarthritis
☐	Greater trochanteric pain syndrome
☐	Meralgia paraesthetica

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☐	Meralgia paraesthetica

Next question

Greater trochanteric pain syndrome is now the preferred term for trochanteric bursitis.

Whilst the x-ray shows joint space narrowing this is not an uncommon finding. Osteoarthritis would also be less likely given the palpable nature of the pain and relatively short duration of symptoms.

Answer D

Q

A 28-year-old woman with rheumatoid arthritis asks for advice about conception. Which one of the following statements is true?

- Methotrexate may be continued during pregnancy as long as the woman takes folic acid 5mg daily**
- NSAIDs should be avoided in the first and second trimester**
- Woman with rheumatoid should be encouraged to conceive as soon as possible (ideally within 1 year) after diagnosis to minimise the risk of complications**
- TNF- α blockers are absolutely contraindicated in pregnancy**
- Hydroxychloroquine is considered safe during pregnancy**

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Rheumatoid arthritis in pregnancy:

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- 10) patients should be referred to an obstetric anaesthetist due to the risk of atlanto-axial subluxation

A 32-year-old woman presents with a facial rash that appears to be worse in summer. She has also noticed intermittent swelling of the small joints of her hands and describes suffering from Raynaud's syndrome for 5 years.

Given the likely diagnosis which of these auto-antibodies is most specific for this condition?

Anti-Ro

Anti-Sm

Anti-nuclear cytoplasmic antibodies

Anti-dsDNA

Anti-nuclear antibodies

A: B

This lady presents with a photosensitive rash, Raynaud's syndrome and small joint arthritis - giving a likely diagnosis of systemic lupus erythematosus (SLE).

Anti-Sm are the most specific antibodies for SLE (up to 99%), but are only found in around 35% of patients with lupus.

Anti-dsDNA antibodies are also highly specific (around 97%) and are positive in around 70% of SLE cases

Anti-nuclear (ANA) antibody is the most likely antibody to be present. 95% of people with SLE have a positive ANA, however it is not very specific.

Anti-Ro antibodies are present in 15% of patients with SLE, but are more frequently associated with Sjögren's syndrome.

Anti-nuclear cytoplasmic antibodies are not associated with SLE. They are associated with inflammatory bowel disease and vasculitis such as Wegener's granulomatosis.

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Anti-dsDNA

Anti-nuclear cytoplasmic antibody

Anti-nuclear antibody

Anti-Sm

Anti-Ro

A: C

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Anti-Sm are the most specific antibodies for SLE, but only around 35% of patients with SLE will be positive. Anti-dsDNA antibodies are positive in around 70% of SLE cases.

Anti-Ro antibodies are present in 15% of patients with SLE, but are more frequently associated with Sjögren's syndrome.

Anti-nuclear cytoplasmic antibodies are not associated with SLE. They are associated with inflammatory bowel disease and vasculitis such as Wegener's granulomatosis.

A 72-year-old woman presents with a severe right-sided headache and some blurring of vision that comes and goes. She has no significant past medical history. On examination, there is tenderness on palpation of her right temporal region. Visual acuity is 6/36 in her right eye and 6/9 in her left.

Investigations: Erythrocyte sedimentation rate 154mm/hr (1-36)

C-reactive protein 116mg/L (<10) What drug should be given initially?

Cyclosporine (intravenous)

Leflunomide (oral)

Methotrexate (oral)

Prednisolone (oral)

Methylprednisolone (intravenous)

A: E

This patient has temporal arteritis, also known as giant cell arteritis (GCA).

The American College of Rheumatology 1990 criteria requires 3 of the following for GCA diagnosis:

1. Age >50 y/o
2. New onset localised headache
3. Temporal artery tenderness or decreased pulsation
4. ESR >50mm/hr
5. Temporal artery biopsy positive

Uncomplicated GCA (no visual involvement and/or jaw/tongue claudication) should be treated with oral prednisolone 40-60mg daily until symptoms and investigations normalise.

Complicated GCA (with visual involvement and/or jaw/tongue claudication), as in this scenario, should be given IV methylprednisolone 500-1000mg for 3 days before starting oral prednisolone.

As GCA requires long-term steroid therapy bone sparing agents (a bisphosphonate and vitamin D) and a gastroprotective drug (e.g omeprazole) should be prescribed. Also, low dose aspirin should be considered as it has been shown to reduce the rate of visual loss and cerebrovascular accidents in GCA.

(Source: Royal College of Physicians guidelines)

<https://www.rcplondon.ac.uk/guidelines-policy/diagnosis-and-management-giant-cell-arteritis>

A 78-year-old man is investigated for headaches. A routine blood screen is normal other than an elevated ALP. A skull x-ray is ordered:



What is the most likely diagnosis?

Myeloma

Cervical spondylosis

Pituitary tumour

Calcified temporal arteritis

Paget's disease of the bone

A: E

The radiograph demonstrates marked thickening of the calvarium. There are also ill-defined sclerotic and lucent areas throughout. These features are consistent with Paget's disease.

Paget's disease

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

increasing age

male sex

northern latitude
family history

Clinical features - only 5% of patients are symptomatic

bone pain (e.g. pelvis, lumbar spine, femur)

classical, untreated features: bowing of tibia, bossing of skull

raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal

skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity,
fracture, periarticular Paget's

bisphosphonate (either oral risedronate or IV zoledronate)

calcitonin is less commonly used now

Complications

deafness (cranial nerve entrapment)

bone sarcoma (1% if affected for > 10 years)

fractures

skull thickening

high-output cardiac failure



elvic x-ray from an elderly man with Paget's disease. There is a smooth cortical expansion of the left hemipelvic bones with diffuse increased bone density and coarsening of trabeculae.



The radiograph demonstrates marked thickening of the calvarium. There are also ill-defined sclerotic and lucent areas throughout. These features are consistent with Paget's disease

A middle aged woman presents with progressive shortness of breath. Chest X ray shows bilateral hilar lymphadenopathy.

Calcium 2.7mmol/l

Angiotensin converting enzyme 200µg/l (<40µg/l)

Given the likely diagnosis, which of the following features would be associated with a good prognosis?

Lupus pernio

Hypercalcaemia

Age>40

Erythema nodosum

HLA B13 subtype

A: D

This woman has sarcoidosis. Factors associated with a good prognosis include HLA B8 and Lofgren's syndrome (bilateral hilar lymphadenopathy, erythema nodosum, polyarthritits and fever). All the other factors listed above are associated with a poor prognosis.

Sarcoidosis

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent. Sarcoidosis remits without treatment in approximately two-thirds of people

Factors associated with poor prognosis

insidious onset, symptoms > 6 months

absence of erythema nodosum

extrapulmonary manifestations: e.g. lupus pernio, splenomegaly

CXR: stage III-IV features

black people

A 30-year-old woman presents with bilateral proximal muscle weakness. She is noted to have blanching of the fingers, especially in cold weather.

Anti-Jo-1 positive

ANA positive

CK 2000 U/L

ESR 60 mm/hr

EMG myopathic changes

The presence of which of the following conveys the worst prognosis?

Dysphagia

Skin rash

CK >2000 U/L

Interstitial lung disease

Raynaud's phenomenon

A: D

Polymyositis is a type of inflammatory myopathy related to dermatomyositis and inclusion body myositis. The hallmark of polymyositis is weakness and/or loss of muscle mass in the proximal musculature, and absent skin involvement. The classic laboratory finding is a raised creatinine kinase (CK) and the Anti-Jo-1 antibody.

Interstitial lung disease (ILD) has a major effect on morbidity and mortality in patients with polymyositis. ILD is considered to be a major risk factor for premature death in patients with myositis.

The anti-Jo-1 antibody is a predictor of the presence of ILD at diagnosis, with up to 70% of patients with the antibody having concurrent ILD. The 5-year survival rate is between 60 and 80%.

Polymyositis

- Overview

- inflammatory disorder causing symmetrical, proximal muscle weakness thought to be a T-cell mediated cytotoxic process directed against muscle fibres

- may be idiopathic or associated with connective tissue disorders associated with malignancy
- dermatomyositis is a variant of the disease where skin manifestations are prominent, for example a purple (heliotrope) rash on the cheeks and eyelids
- typically affects middle-aged, female : male 3:1
- Features
 - proximal muscle weakness +/- tenderness
 - Raynaud's
 - respiratory muscle weakness
 - interstitial lung disease: e.g. fibrosing alveolitis or organising pneumonia
 - dysphagia, dysphonia
- Investigations
 - elevated creatine kinase
 - EMG
 - muscle biopsy
 - anti-Jo-1 antibodies are seen in pattern of disease associated with lung involvement, Raynaud's and fever

A 20-year-old Nigerian female presents to the Emergency Department with chest pain. She reports a long history of fatigue and joint pains. Examination reveals a pericardial rub and bilateral pitting oedema. Observations show only that she has a low grade pyrexia 37.7°C and blood pressure 170/100 mmHg. Urinalysis shows haematuria and nephrotic-range proteinuria. A urine pregnancy test is negative. ECG shows saddle-shaped ST-elevation in all leads. Of interest, her blood results show:

Urea 8.2 mmol/l

Creatinine 212 µmol/l

eGFR 33ml/m/m²

Which of the following histopathological findings is most likely on renal biopsy?

Focal proliferative glomerulonephritis

Membranous glomerulonephritis

Diffuse proliferative glomerulonephritis

Focal segmental glomerulosclerosis

Mesangial proliferative glomerulonephritis

A: C

This question requires you to diagnose the condition and then recall the associated histopathology. Although they may not be encountered every day in clinical practice, the glomerulonephritides are favourites of the MRCP examiners.

The presence of hypertension, kidney injury, proteinuria and haematuria point towards a nephritic picture of kidney insult.

The multisystem presentation of fever, arthralgia, pericarditis and nephritis associated with the epidemiological clues (a young black female) suggest in this case a diagnosis of systemic lupus erythematosus (SLE).

SLE: renal complications

WHO classification

class I: normal kidney

class II: mesangial glomerulonephritis

class III: focal (and segmental) proliferative glomerulonephritis

class IV: diffuse proliferative glomerulonephritis

class V: diffuse membranous glomerulonephritis

class VI: sclerosing glomerulonephritis

Class IV (diffuse proliferative glomerulonephritis) is the most common and severe form. Renal biopsy characteristically shows the following findings:

- glomeruli shows endothelial and mesangial proliferation, 'wire-loop' appearance
- if severe, the capillary wall may be thickened secondary to immune complex deposition
- electron microscopy shows subendothelial immune complex deposits
- granular appearance on immunofluorescence

A 66-year-old female with COPD and a background of multiple previous courses of steroids presents to her GP for a routine bloods screen. She also has hypertension and angina. Her blood results are as follows:

25-OH Vitamin D 16 nmol/l (>50)

Adjusted calcium 2.34 mmol/l

Her dietary intake of calcium is good. Which answer is most appropriate in view of her past medical history and vitamin D levels?

Give calcium and vitamin D combined

Reassurance

Repeat in 1 year and if vitamin D <10 commence treatment

Commence oral bisphosphonate

Oral vitamin D loading then maintenance

A: E

This patient has vitamin D deficiency and thus the correct answer is to load with vitamin D and then continue on maintenance. In patients with good calcium intake and normal serum calcium, giving oral calcium may actually be detrimental.

This is due to evidence suggesting adverse cardiovascular outcomes, which is thought to be related to accelerated tissue and vascular calcification. Thus given her background of angina, this should be avoided.

Measurement of serum 25-OH vitamin D is the best way of estimating vitamin D status.

Optimal: > 75nmol/l

Adequate: 50-75nmol/l

Insufficiency: 30-49nmol/l

Deficiency: < 30nmol/l

Serum 25OHD < 30 nmol/l: treatment recommended

Serum 25OHD 30-50 nmol/l: treatment is advised in patients with: fragility fracture, osteoporosis, symptoms suggestive of vitamin D deficiency, reduced exposure to sunlight, raised PTH, conditions associated with malabsorption

Serum 25OHD > 50 nmol/l: provide reassurance and give advice on maintaining adequate vitamin D levels through safe sunlight exposure and diet

Vitamin D supplementation

- Vitamin D supplementation has been a hot topic for a number of years now.

- The muddied waters are now slightly clearer following the release of the following:
 - 2012: letter by the Chief Medical Officer regarding vitamin D supplementation
 - 2013: National Osteoporosis Society (NOS) release UK Vitamin D guideline
- The following groups should be advised to take vitamin D supplementation:
 - all pregnant and breastfeeding women should take a daily supplement containing 10µg of vitamin D
 - all children aged 6 months - 5 years. Babies fed with formula milk do not need to take a supplement if they are taking more than 500ml of milk a day, as formula milk is fortified with vitamin D
 - adults > 65 years
 - 'people who are not exposed to much sun should also take a daily supplement'

Testing for vitamin D deficiency

The key message is that not many people warrant a vitamin D test. The NOS guidelines specify that testing may be appropriate in the following situations:

- patients with **bone diseases** that may be improved with vitamin D treatment e.g. known osteomalacia or Paget's disease
- patients with bone diseases, **prior to specific treatment** where correcting vitamin deficiency is appropriate e.g, prior to intravenous zoledronate or denosumab
- patients with **musculoskeletal** symptoms that could be attributed to vitamin D deficiency e.g. bone pain ?osteomalacia
- Patients with **osteoporosis** should always be given calcium/vitamin D supplements to testing is not considered necessary. People who are at higher risk of vitamin D deficiency (see above) should be treated anyway so again testing is not necessary.

VITAMIN D - ADVICE ON SUPPLEMENTS FOR AT RISK GROUPS

<https://www.nos.org.uk/document.doc?id=1352>

Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213703/dh_132508.pdf

A 41-year-old woman presents with tightening of fingers, mild difficulty swallowing, and mild shortness of breath on exertion. She takes pantoprazole for reflux. On examination there is tightening of skin in her fingers, however the rest of the skin is normal. Her joints are not inflamed. The rest of her examination was normal (including chest examination). Her chest X-ray is also normal. There is mild decrease in DLCO on lung function tests. Which of the following antibodies are indicative of the underlying diagnosis?

Anti-Scl-70 antibody

Anti-dsDNA antibody

Rh factor antibody

Anti-centromere antibody

Anti-Jo-1 antibody

A: D

The underlying diagnosis is limited scleroderma. Limited scleroderma has tightened hard skin below the elbows. Dysphagia and some lung fibrosis occurs in both limited and diffuse scleroderma.

Limited scleroderma is associated with anti-centromere antibody with Anti-scl-70 antibody associated with diffuse scleroderma.

Diffuse scleroderma is characterised by lesions proximal to the elbow, trunk and face (limited can have some facial involvement)

Limited scleroderma has a 90% 5-year survival, diffuse scleroderma 70% 5-year survival

In the past, renal crises were the most common cause of death in patients with scleroderma. Aggressive treatment with blood pressure lowering drugs, particularly those known as ACE inhibitors, is proving to be successful in reducing this risk.